UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(D)
OF THE SECURITIES EXCHANGE ACT OF 1934

Date of Report (Date of earliest event reported): July 16, 2021

TEMPEST THERAPEUTICS, INC.

(Exact name of Registrant as Specified in its Charter)

Delaware	**001-35890**	**45-1472564**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

7000 Shoreline Court, Suite 275
South San Francisco, CA 94080
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (415) 798-8589

N/A
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001 per share	**TPST**	**The Nasdaq Capital Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events.

Business Section and Risk Factors of the Company

As previously disclosed, on June 25, 2021, the Company completed a merger with TempestTx, Inc. (formerly Tempest Therapeutics, Inc.) ("Tempest") in accordance with the terms of the Agreement and Plan of Merger, dated as of March 29, 2021 (the "Merger Agreement"), by and among the Company, Tempest and Mars Merger Corp., a Delaware corporation and a wholly owned subsidiary of the Company ("Merger Sub"), pursuant to which, among other matters, Merger Sub merged with and into Tempest, with Tempest continuing as a wholly owned subsidiary of the Company and the surviving corporation of the merger (the "Merger").

The Company is filing this Current Report on Form 8-K to provide (1) an updated business description of the Company, which is attached hereto as Exhibit 99.1 and incorporated herein by reference and (2) updated risk factors, which are attached hereto as Exhibit 99.2 and incorporated herein by reference.

Management's Discussion and Analysis of Tempest and Certain Financial Information of Tempest

The Company is also providing Tempest's management's discussion and analysis for the quarter ended March 31, 2021, which is attached hereto as Exhibit 99.3 and incorporated herein by reference. Tempest's corresponding unaudited condensed interim financial statements as of March 31, 2021 and for the three months ended March 31, 2021, were included our Current Report on Form 8-K/A filed on July 1, 2021.

The Company is also filing this Current Report on Form 8-K to provide Tempest's historical audited financial statements for the year ended December 31, 2020 and 2019 (the "Tempest Financial Statements"), and the unaudited pro forma combined financial information for Millendo and Tempest for the year ended December 31, 2020 (Unaudited Pro Forma Condensed Combined Financial Information), which were both originally reflected in the Registration Statement on Form S-4/A filed on May 10, 2021 (which Registration Statement is not incorporated by reference in or a part of this Current Report on Form 8-K). The Tempest Financial Statements and the Unaudited Pro Forma Condensed Combined Financial Information are attached hereto as Exhibit 99.4 and Exhibit 99.5, respectively, and incorporated herein by reference.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements (including within the meaning of Section 21E of the Exchange Act and Section 27A of the Securities Act of 1933, as amended (the "Securities Act")) concerning us, Tempest and the Merger. These statements may discuss goals, intentions and expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of our management, as well as assumptions made by, and information currently available to, our management. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as "may," "will," "should," "would," "expect," "anticipate," "plan," "likely," "believe," "estimate," "project," "intend," and other similar expressions. Statements that are not historical facts are forward-looking statements. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Exhibit Description
23.1	Consent of Deloitte & Touche LLP for Tempest
99.1	Company Business Section
99.2	Company Risk Factors
99.3	Management's Discussion and Analysis of Tempest for the Quarterly Period ended March 31, 2021
99.4	Audited Financial Statements of Tempest as of December 31, 2020 and 2019
99.5	Unaudited Pro Forma Condensed Combined Financial Information

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

TEMPEST THERAPEUTICS, INC.

Date: July 16, 2021

By: /s/ Stephen Brady
Name: Stephen Brady
Title: Chief Executive Officer

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-228209 and 333-230749 on Form S-3 and Registration Statement Nos. 333-182040, 333-187897, 333-195780, 333-202793, 333-209775, 333-214414, 333-216405, 333-221292, 333-226750, 333-230749, 333-230750, 333-235515, 333-249993, 333-255261, and 333-257727 on Form S-8 of our report dated May 10, 2021, relating to the financial statements of Tempest Therapeutics, Inc. appearing in this Current Report on Form 8-K dated July 16, 2021.

/s/Deloitte & Touche LLP

San Francisco, California
July 16, 2021

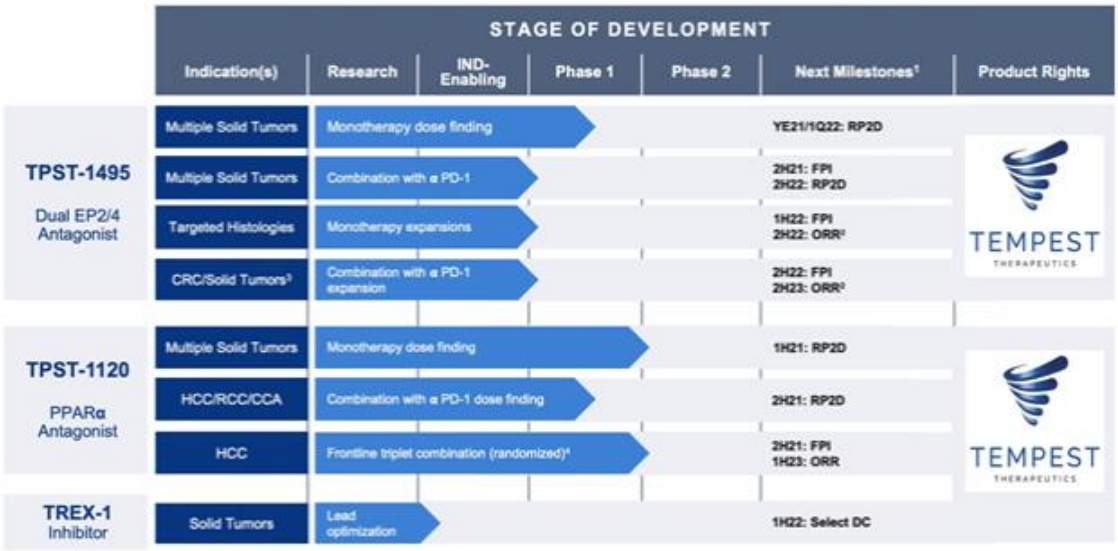
TEMPEST'S BUSINESS

Overview

Tempest is a clinical-stage oncology company focused on leveraging its deep scientific understanding of cancer biology and medicinal chemistry to develop and advance novel, orally available therapies for the treatment of solid tumors. Tempest's philosophy is to build a company based upon not only creative science and thoughtful management, but also upon the efficient translation of those ideas into therapies that will improve patient's lives. To this end, Tempest is advancing TPST-1495 and TPST-1120, two product candidates in clinical trials that it believes are the first clinical-stage molecules designed to treat their respective targets; and a third program in preclinical studies that could be the first to target TREX-1, a key cellular enzyme that regulates the innate immune response in tumors. TPST-1495 is a dual antagonist of EP2 and EP4, receptors of prostaglandin E2, and is currently in a Phase 1 trial in solid tumors. Tempest's second program, TPST-1120, is a selective antagonist of peroxisome proliferator-activated receptor alpha, or PPARα, and is also in a Phase 1 trial in solid tumors. Tempest expects to report initial data from both these programs in the first half of 2022. Additionally, Tempest is advancing a third program targeting the three prime repair exonuclease, or TREX-1, for which Tempest expects to select a development candidate in the first half of 2022. Beyond these three ongoing programs, Tempest plans to leverage its drug development and company-building experience, along with academic relationships, to identify promising new targets that may feed new programs into Tempest's pipeline.

Tempest's Pipeline

Tempest has developed a diversified pipeline of small molecule product candidates that Tempest believes are innovative and target scientifically validated pathways. These product candidates are designed to target tumor cells directly, modulate the immune system to kill cancer cells, or a combination of both. Tempest selected targets that are expressed in a diverse set of tumor types, with the intention to address unmet medical needs or improve existing standards of care. Tempest's product development programs consist of the following:



Definitions:

HCC: hepatocellular carcinoma; RCC: renal cell carcinoma; CCA: cholangiocarcinoma; CRC: colorectal cancer; FPI: First Patient In; RP2D: Recommended Phase 2 Dose; DC: Development Candidate; ORR: Objective Response Rate. Note that the primary anti-tumor activity readout is ORR by RECIST v. 1.1 criteria, and time on study treatment; additional endpoints include duration of response and progression free survival, which may be reported at a later timepoint.

[1] Timing is an estimate is based on projections for internal receipt of data (not necessarily external release); an event may not result in a change in company value. [2]The company is evaluating both patient-targeted and histology-based arms, for which a subset of the data could be available as early as 2H22, with additional data in 2023. [3]The company is evaluating if the combination expansion will focus on CRC or a set of targeted solid tumors. [4] Pursuant to a collaboration with Roche; TPST retains all product rights

Tempest's Program Summaries

Tempest's first product candidate is TPST-1495, a novel, oral, small molecule designed to be a dual antagonist of only two of the four prostaglandin E2 (PGE2) receptors, EP2 and EP4, sparing the homologous—but differentially active—EP1 and EP3 receptors. To our knowledge, TPST-1495 is the first dual EP2/EP4 PGE2 receptor antagonist in the clinic. PGE2 is well understood from the scientific literature to be an important stimulator of tumor growth in diverse cancer types of high need, and to be inhibitory to anti-tumor immune function in the tumor microenvironment. PGE2 signaling through EP2 and EP4 has been observed both to enhance tumor progression and promote immune suppression. Tempest conducted head-to-head preclinical studies comparing TPST-1495 to single antagonists of EP4 being developed by other companies. In these studies, Tempest observed significantly enhanced activity of TPST-1495 in both overcoming PGE2-mediated suppression of human immune cells in vitro as well as significantly increased anti-tumor activity in mouse models of human colorectal cancer, as compared to single antagonists of EP4. Tempest is currently evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and possible anti-tumor activity of TPST-1495 in a multicenter Phase 1a/1b dose and schedule optimization study in subjects with advanced solid tumors, with a focus on prostaglandin-driven tumor types, such as colorectal cancer, or CRC. Tempest is observing dose-proportional exposure, and Tempest is encouraged by early signs of activity of TPST-1495 monotherapy, as shown by on-target pharmacodynamic changes, disease control, and reduction of tumor-specific biomarkers in the ongoing dose optimization clinical study. The TPST-1495 Phase 1 clinical trial is ongoing in the schedule and dose optimization stage and Tempest expects to establish the RP2D for expansion and the preliminary safety profile and ORR in first half of 2022. Tempest also expects to initiate monotherapy combination studies with an anti-PD-1/L1 immune check point inhibitor, prior to the end of 2021.

Tempest's second product candidate is TPST-1120, an oral, small molecule designed to be a selective antagonist of PPARα and is the first PPARα antagonist in the clinic. PPARα is a key transcription factor controlling fatty acid oxidation, or FAO. It is clear from the scientific literature that FAO can serve as a source of energy for tumor cell growth and that the PPARα transcriptome is upregulated in many tumor types. It also is published that FAO is a preferred energy source for so-called immune suppressor cells such as regulatory T-cells (Treg), myeloid derived suppressor cells, or MDSCs, and M2 macrophages. Tempest's preclinical data suggest that TPST-1120 can directly kill tumor cells that are dependent upon FAO, alter the tumor microenvironment immune cell infiltrate away from a suppressor immune phenotype, and synergize with immune checkpoint inhibitor therapy in animal models. Tempest is evaluating TPST-1120 in a Phase 1a/b clinical study that has both monotherapy and combination therapy arms in patients with advanced solid tumors that Tempest's PPARα-dependent transcriptome analysis of diverse human cancers revealed favor the usage of FAO. Tempest has been observing dose-dependent exposure and on-target pharmacodynamic changes in both monotherapy and combination TPST-1120 therapy arms. The monotherapy dose escalation phase of the clinical study has been completed, and Tempest observed clinical benefit in 10 of 20 of patients enrolled in this arm in the form of disease stabilization. Three patients with advanced cholangiocarcinoma experienced prolonged stable disease (^{3}21 weeks) and some reduction of tumor burden, although not to the extent of a RECIST response. In the TPST-1120 combination arm with nivolumab, Tempest observed a deep and durable RECIST response in a patient with 4th line kidney cancer that had previously failed to respond to, and then progressed on, the combination immune-oncology, or IO, regimen of nivolumab with ipilimumab. This patient experienced a rapid tumor reduction to -54% by RECIST criteria on TPST-1120 + nivolumab at the first on-treatment assessment at eight weeks, which has subsequently deepened to -61% after six months of treatment and is ongoing. Tempest is encouraged by this response as a signal of synergy between TPST-1120 and anti-PD-1 therapy in IO-resistant disease. In March 2021, Tempest announced a clinical collaboration with Hoffman-La Roche Ltd., or Roche, to accelerate the development of TPST-1120 into a frontline, randomized study. Pursuant to the terms of Tempest's collaboration, Roche will evaluate TPST-1120 in a global randomized phase 1b/2 clinical study in combination with the standard-of-care first-line regimen of atezolizumab and bevacizumab in patients with advanced or metastatic hepatocellular carcinoma, or HCC, not previously treated with systemic therapy. The study will include at least 40 and up to 60 patients who will receive the TPST-1120 combination and will be compared to the standard-of-care atezolizumab and bevacizumab regimen with primary objectives of anti-tumor activity and safety. Under the terms of the collaboration agreement, Roche will manage the study operations for this global multicenter trial. Tempest will retain global development and commercialization rights to TPST-1120. Tempest expects the first patient in the frontline HCC study to be enrolled in mid-2021, and for ORR results of the TPST-1120 Phase 1a/1b dose finding trials to be available by early 2022.

Tempest has a third program in its pipeline against TREX-1, a target Tempest believes may be an effective approach to modulate STING, which stands for **ST**imulator of **IN**terferon **G**enes, with a systemic therapy. The STING pathway is the focus of clinical and pre-clinical programs at multiple pharmaceutical and biotechnology companies. TREX-1 is a double-stranded DNA exonuclease that controls activation of the cGAS/STING pathway, which is an innate immune response pathway that induces the production of IFN-ß, a cytokine that is well-established to be a key factor in triggering the development of anti-tumor immunity. The expression of TREX-1 is enhanced in tumors and inhibits activation of cGAS/STING to evade immune recognition. Because STING is expressed ubiquitously, but TREX-1 expression is increased in tumors, Tempest believes that TREX-1 may be the optimal approach to target STING with an orally available small molecule inhibitor to selectively activate this pathway in tumors. Tempest has demonstrated proof of concept of this approach in a mouse tumor model with a TREX-1 inhibitor tool compound and expects to select a TREX-1 inhibitor development candidate for IND-enabling studies in the first half of 2022.

Our Internal Discovery Capability and Team

Tempest built an internal discovery team at Tempest to create and advance small-molecule product candidates with the ideal pharmacological properties to target the tumor micro-environment and/or leverage the immune system. This discovery capability has enabled what Tempest believes is the rapid and efficient generation of a broad pipeline of innovative, orally available therapies, that if approved by the FDA, will be first-in-class. Tempest's small molecule product candidates target pathways that have been validated in the scientific literature to play key roles in promoting tumor growth and suppressing anti-tumor immunity across a diverse set of cancers.

Tempest leveraged its deep scientific knowledge, long-term established relationships with key opinion leaders, and extensive medicinal chemistry and drug development expertise to develop its current portfolio. Dr. Peppi Prasit, a Tempest founder, serves a continuing role in the design of Tempest's small molecule therapeutics. Dr. Prasit (see also under Scientific Advisors) has direct involvement in both Tempest's medicinal chemistry activities and synthetic chemistry activities conducted by contract research organizations. Dr. Prasit has played a pivotal role in the discovery of multiple marketed drugs, including Vioxx® and Arcoxia® while at Merck Frosst, and led the medicinal chemistry of several drugs still under clinical development. Tempest believes that the expertise that Dr. Prasit imparts on the development of its small molecule drugs is a differentiating factor of the potential activity of its product candidates. Tempest designs its molecules to have the ideal pharmacological properties for the targeted pathway and the desired clinical effect. Small-molecule drugs against the same biological target can be highly differentiated from each other based on their respective pharmacokinetic, pharmacodynamic and biophysical properties. For example, many small-molecule drugs are potent when tested in buffer solution but lose a significant amount of potency in physiologically relevant media, such as blood or tumor tissue. Tempest rigorously tests its molecules in whole blood or other physiologically relevant systems and only advances molecules that retain a high degree of activity when tested under such "real world" conditions.

For instance, the Tempest team leveraged Dr. Prasit's scientific insights gained from developing approved prostaglandin signaling pathway targeted drugs, together with the published literature, to hypothesize that optimal anti-tumor inhibition and immune activation might result from blocking both EP2 and EP4 receptor signaling pathways. Tempest designed TPST-1495 to be a first-in-class dual selective inhibitor of prostaglandin receptors EP2 and EP4 based on this scientific hypothesis. Tempest established the scientific rationale for developing TPST-1120 after discussions with several academic investigators, including Dr. David Spaner, MD, PhD (Sunnybrook Research Institute, Toronto), who found that patients with selected advanced cancers had comparatively elevated levels of long-chain fatty acid amides in peripheral blood that were reduced after responding to approved therapies. These findings, along with the published literature demonstrating the role of lipid metabolism on metastasis, angiogenesis and immune evasion, led Tempest to establish an internal program to develop selective antagonists of PPARα, a transcription factor that regulates lipid metabolism. This pathway is known to be druggable, with the decades-long clinical use of fenofibrates, a class of small molecule PPARα agonists, in patients with dyslipidemia. In addition, several members of the team at Tempest developed the first-in-human small molecule STING agonists at a prior company. The Tempest president, Dr. Tom Dubensky, is recognized as a thought leader in drugging the STING pathway. The insights and experience of the Tempest team, together with the rapidly expanding scientific understanding of the role of innate immunity in developing effective tumor-specific immunity, led Tempest to the scientific hypothesis that the optimal approach to localize activation of the STING pathway to the tumor microenvironment in metastatic disease with an orally available small molecule is through a specific inhibitor of TREX-1, a dsDNA exonuclease known to have elevated expression in tumors. The Tempest team is actively considering other innovative oncology targets that it believes have strong scientific rationale and would address specific unmet medical needs.

The Tempest senior management team, comprised of Steve Brady, CEO, Tom Dubensky, PhD, President, and Sam Whiting, MD, PhD, CMO, possess extensive experience gained over many years in both private and public biotechnology companies in the selection of new targets, discovery of molecules to modulate pathways of interest, and the evolution of program candidates through the full range of clinical development. The team also has substantial financing and strategic transaction experience, including private and public equity and debt financings, product and licensing collaborations, and both private and public M&A. Tempest believes the collective and diverse experience of the team, along with Tempest's view that a company should be run in accordance with a foundational set of guiding principles, positions the company for success in developing therapies to benefit patients living with cancer. While Tempest believes that its experienced management team represents an important competitive advantage, the historical results, past performance and/or acquisition of companies with which members of its management team have been affiliated do not necessarily predict or guarantee similar results for its company.

Our scientific and clinical advisors includes thought leaders in oncology, immunology and clinical development, including: Toni K. Choueiri, MD, Director, Lank Center for Genitourinary Oncology, Department of Medical Oncology, Dana-Farber Cancer Institute and Co-Leader, Kidney Cancer Program, Dana-Farber/Harvard Cancer Center; Drew M. Pardoll, MD, PhD, Abeloff Professor of Oncology, Director, Bloomberg–Kimmel Institute for Cancer Immunotherapy, Director, Cancer Immunology Program, Johns Hopkins University School of Medicine; Jason Luke, MD, FACP, Associate Professor of Medicine, Hematology/Oncology, and Director of the Cancer Immunotherapeutics Center within the UPMC Hillman Cancer Immunology and Immunotherapy Program; Raymond N. Dubois, MD, PhD, Dean of the College of Medicine at the Medical University of South Carolina; Peppi Prasit, PhD, CEO Emeritus Inception Sciences; Russell Vance, PhD, Professor and HHMI Investigator, University of California, Berkeley; and, Benjamin F. Cravatt, PhD, Professor and Gilula Chair of Chemical Biology, Department of Chemistry, The Scripps Research Institute. Tempest additionally has extensive established relationships with key opinion leaders, or KOLs, with whom Tempest has sponsored research agreements and/or frequently consult to both gain insights on Tempest's existing pipeline and clinical development strategy and to discuss potential new target opportunities.

As of July 9, 2021, Tempest had 15 employees, including nine holding Ph.D., M.D., JD, LL.M., and/or MBA degrees, and have established internal expertise in chemistry, biochemistry, molecular biology, immunology, pharmacology, toxicology, pre-clinical development, regulatory and quality, translational medicine, and early-to-late-stage clinical development, as well as finance, business development and strategic transactions. An important element of Tempest's strategy to date has been to utilize consultants with whom Tempest has established relationships over several companies and in the development of multiple innovative oncology therapies, including those skilled in medicinal chemistry, pharmacology and toxicology, translational sciences, clinical operations and medical affairs. Tempest will continue to maintain internal capabilities in R&D and clinical development areas as noted and add experienced and talented scientists in areas, such as medicinal chemistry, that Tempest believes are critical for the discovery of highly differentiated small-molecule compounds. Additionally, while Tempest's current pipeline consists of orally-available small molecules, the Tempest team is also experienced in the conception, translation and clinical development of simple and complex biologics.

Tempest's Strategy

The Tempest team has come together to build an integrated company that delivers meaningful therapies to cancer patients, through leveraging its team's capabilities and research and development engine. Tempest expects to build value for the Tempest shareholders with the following over-arching strategy:

- *Effectively advance TPST-1495, its dual EP2/4 antagonist, through clinical development to meaningful data*. Tempest plans to complete the TPST-1495 monotherapy dose and optimization stage of the ongoing Phase 1 study in the second of half of 2021, followed by the initiation of monotherapy dose expansion in targeted patient populations, as well as the combination of TPST-1495 with an immune checkpoint inhibitor. Tempest expects to have ORR data from the monotherapy dose and optimization cohort beginning in the first half of 2022, followed by data from the other cohorts beginning in the second half of 2022.
- *Facilitate Tempest's Roche collaboration evaluating TPST-1120 in a randomized, frontline HCC study*. Pursuant to the terms of its agreement with Roche, Tempest expects Roche to commence enrollment of patients in mid-2021, and for enrollment to be complete by the end of 2022. Because TPST-1120 is being combined with a standard-of-care first line treatment and randomized against that same standard-of-care, Tempest believes that positive study results may provide multiple strategic opportunities.
- *Advance its TREX-1 inhibitor into clinical studies*. The Tempest team developed the first-in-human STING agonists in a prior company and are widely acknowledged to be leaders in this pathway. Tempest believes that a selective TREX-1 inhibitor given orally will be an effective approach to engage the STING pathway broadly in the tumor microenvironment of metastatic disease. Tempest's medicinal chemists have developed a series of compounds with low nanomolar potency against human TREX-1, which Tempest is actively optimizing towards selecting a development candidate for IND enabling activities in the first half of 2022.
- *Explore business development opportunities to maximize the potential of its pipeline and extend financial resources*. Tempest believes that its pipeline has broad potential, and partnerships that bring additional expertise and/or geographic presence could be important aspects of its progress. Tempest established a clinical collaboration with Roche to evaluate TPST-1120 in a global frontline randomized study in HCC patients, which Tempest believes accelerated the program by years without the risk of the associated global infrastructure build, while retaining global development and commercialization rights. Tempest intends to become a fully integrated biopharmaceutical company and build a targeted sales force in the United States to support the commercialization of its drug candidates, if approved.
- *Enhance Tempest's pipeline by identifying novel oncology targets and in-licensing promising product candidates for oncology.* Tempest is actively evaluating and pursuing novel targets, intellectual property and product candidates for acquisition and in-licensing to supplement Tempest's internal research efforts and continue to build its pipeline of targeted molecules for oncology. Through the team's focus and expertise in oncology and immunology, as well as established relationships with oncology and immunology thought leaders, Tempest is positioning itself as a partner of choice for innovative oncology drug candidate development. Tempest believes continued advances in the biological understanding of diseases will provide opportunities to further expand its portfolio with preclinical and/or clinical product candidates.

Our programs

TPST-1495: Dual EP2/EP4 Prostaglandin Receptor Antagonist

Program Summary

Our first clinical molecule is TPST-1495, a potentially first-in-class, oral, small molecule dual antagonist of the PGE2 receptors, EP2 and EP4. TPST-1495 is engineered to inhibit only the EP2 and EP4 receptors while sparing the homologous—but differentially active—EP1 and EP3 receptors. There is extensive literature demonstrating that PGE2 both enhances tumor proliferation and inhibits anti-cancer immune function; it is known from the scientific literature that many tumors express elevated levels of the cyclooxygenase enzymes that produce PGE2. The literature supports that PGE2 predominantly drives tumor proliferation by autocrine signaling through EP2 and EP4 receptors on tumor cells and immune suppression through EP2 and EP4 receptors on lymphoid and myeloid immune cells in the tumor microenvironment. Tempest has conducted extensive preclinical studies to test and compare the anti-tumor activities and immune activation of EP2- and EP4-specific inhibition by TPST-1495 to alternative mechanisms of PGE2 inhibition, supporting the improved activity of the TPST-1495 approach. Tempest additionally conducted IND-enabling pharmacology and toxicology studies to support initiation of its ongoing first-in-human Phase 1/1b study of TPST-1495 monotherapy in patients with advanced solid tumors. The company is currently evaluating the safety, tolerability, pharmacokinetics (or PK), pharmacodynamics (or PD) and preliminary anti-tumor activity of TPST-1495 in this multicenter study conducted at Phase 1 units in the United States. Tempest has observed dose-dependent TPST-1495 exposure, on-target pharmacodynamic changes and reduction of tumor-specific biomarkers in the ongoing dose optimization stage of the clinical study. Tempest expects to initiate dose-finding combination studies with anti-PD-(L1) immune checkpoint inhibitor therapy in the second half of 2021 and initiate dose expansion studies with TPST-1495 as monotherapy in targeted patient populations in the first half of 2022.

Prostaglandin E2 enhances tumor progression of diverse cancers

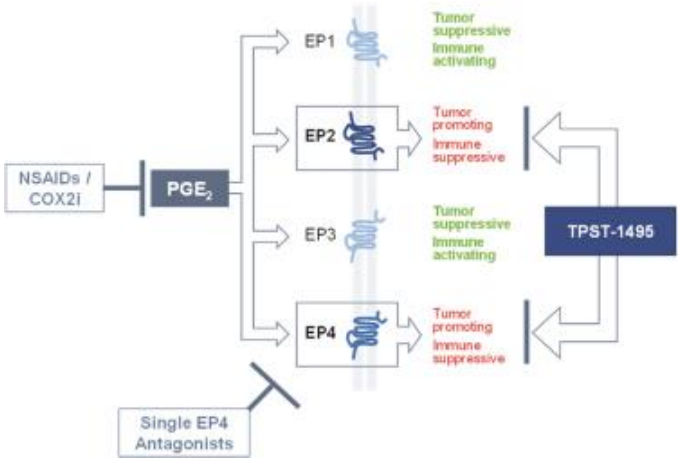
Elevated expression of COX-2 and overproduction of PGE2 is correlated with progression of diverse malignancies by stimulating tumor cell proliferation, survival, evasion and metastasis as well as host angiogenesis. In addition, PGE2 suppresses anti-tumor immunity by inhibiting the function of critical anti-tumor immune effector cell populations such as dendritic cells, natural killer, or NK cells, T cells, and M1 macrophages, while promoting the activity of suppressive immune cell populations, including myeloid-derived suppressor cells, or MDSCs, M2 macrophages, and regulatory T cells. Additionally, recent studies have shown that increased expression of COX-2 and production of PGE2 can play a role in the effectiveness of immune checkpoint inhibitor therapy and in the development of adaptive resistance to therapy. This body of literature provides the scientific rationale for developing therapeutics that maximally inhibit the prostaglandin pathway.

How PGE2 signals through each of its four homologous E-prostanoid G-protein coupled receptor targets, known as EP1, EP2, EP3 and EP4, informed the development of TPST-1495. PGE2 signaling through each of these receptors activates distinct signal transduction pathways. In general, signaling through EP2 and EP4 receptors increases the activity of suppressive immune cell populations found in the tumor microenvironment of metastatic tumors, including myeloid derived suppressor cells, M2 macrophages, regulatory T cells, and exhausted CD8+ T cells. In contrast, EP3 signaling is generally pro-inflammatory and inhibits the activity of EP2 and EP4 receptor signaling. Decreased EP1 and EP3 receptor expression levels has been associated with numerous progressing malignancies. The differential modulation of anti-tumor immune responses by the four individual EP receptors provides the scientific rationale that selective antagonism of only the EP2 and EP4 receptors provides enhanced anti-tumor immunity and improved therapeutic effect, as compared to selective EP4 antagonists or COX-1 or COX-2 inhibitors. Tempest does not believe that preventing signaling through all four EP receptors by inhibiting the production of PGE2 (e.g., with nonsteroidal anti-inflammatory drugs, or NSAIDs, which target both COX-1 and COX-2 or with drugs that target only COX-2) is an optimal therapeutic approach for cancer treatment for two reasons. First, these agents have multiple effects beyond just inhibiting PGE2 production and are associated with renal and cardio toxicities with long-term use, particularly at high doses. Second, and perhaps more importantly, by preventing PGE2 production, these agents prevent PGE2-mediated signaling through EP1 and EP3. Tempest has demonstrated in human immune cell culture systems in vitro that signaling through EP1 and EP3 is required for optimal functional activation of critical immune cell populations required for mounting anti-tumor immunity, such as dendritic cells.

Rationale for Clinical Evaluation of TPST-1495 in Solid Tumors

There is strong evidence in the literature that indicates a role of both EP2 and EP4 in regulating PGE2-mediated immune suppression in the tumor microenvironment, or TME, indicating that effective anti-tumor immunity might be best achieved with a dual EP2/EP4 antagonist. Overall, as a dual antagonist targeting both EP2 and EP4, TPST-1495 offers the potential for unique therapeutic properties as compared to either broad inhibition of PGE2 signaling via COX inhibitors or EP4-specific single antagonists that are currently in clinical development. The Figure below provides a schematic representation for selectively antagonizing both EP2 and EP4 receptors with TPST-1495 and preserving PGE2 signaling through EP1 and EP3 to maintain functional immunity. Increased levels of EP2 and EP4 receptor expression is correlated with tumor progression, most notably in colorectal carcinoma; EP2 and EP4 receptor signaling has also been associated with enhanced tumorigenesis. Subjects with all histologic types of solid tumors are eligible for Tempest’s ongoing Phase 1/1b study of TPST-1495. However, enrollment of subjects with colorectal cancer, non-small cell lung cancer, squamous cell carcinoma of the head and neck, urothelial cancer, endometrial cancer, and gastroesophageal junction or gastric cancer are specified in the protocol as being preferred histologies, as the data from preclinical studies evaluating EP2 and EP4 antagonists in vivo as well as gene expression profiling from primary human tumors (data from the Cancer Genome Atlas) indicate that these tumor types may be particularly susceptible to an anti-EP2 and anti-EP4 dual antagonist.

TPST-1495 Mechanism of Action



TPST-1495 Antagonist Activity is Selective and Specific to EP2 and EP4

Tempest evaluated TPST-1495 as a competitive antagonist to PGE2 signaling in a calcium flux assay against human EP1, EP2, EP3 and EP4 using commercially available cell lines that individually express a single designated EP receptor. PGE2 binding to the four related EP receptors leads to distinct downstream signaling events due to the different G protein coupling status of each receptor. EP1 and EP3 signaling activates calcium flux and EP2 and EP4 signaling stimulates the production of immune suppressive cAMP. In order to use calcium flux as a consistent readout for the binding of all four EP receptors to PGE2, cell lines stably expressing EP2 or EP4 were also transfected with a promiscuous G protein. This enabled the activation of the calcium signaling pathway in response to binding of PGE2 to EP2 and EP4. TPST-1495 did not achieve 50% inhibition of EP1 or EP3 at concentrations up to 30 µM, and the IC50 values in two independent experiments were calculated to be 134,200 nM and 108,800 nM for EP1 and EP3, respectively. In contrast, the calculated IC50 for EP2 was 17.21 nM in 14 independent experiments and 3.24 nM for EP4 in15 independent experiments. Tempest believes that these experimental results indicate that TPST-1495 is a highly selective and specific dual antagonist of EP2 and EP4 PGE2 receptors.

Tempest evaluated TPST-1495 selectivity in vitro in a broad Eurofins Cerep screen of 75 targets, supplemented by additional adenosine transporter binding and uptake assays. In the presence of 10 µM TPST-1495, mean inhibition of specific binding for all binding targets was less than 50% with the exception of the adenosine transporter assay. Tempest believes that these results suggest that TPST-1495 is highly selective and does not significantly bind or affect the activity of a broad range of targets. Tempest subsequently determined that the IC50 for inhibition of adenosine uptake was 0.26 µM, which is approximately 16-fold higher than the observed maximum unbound concentration of 0.016 µM TPST-1495 at a clinical dose of 25 mg.

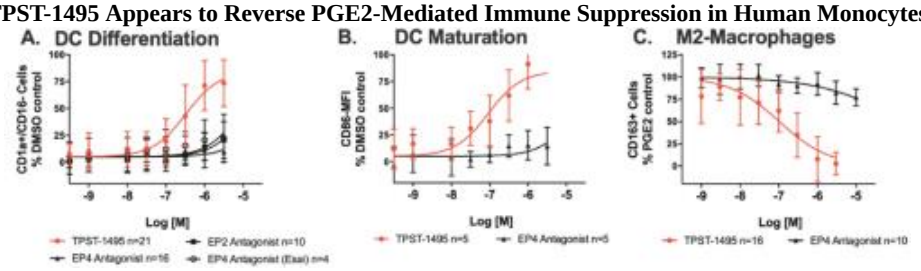
Summary of TPST-1495 Preclinical Results

Tempest conducted an extensive series of in vitro and in vivo experiments to assess the activity of TPST-1495 to support the rationale for its clinical evaluation. In this section Tempest shows some of its experimental results which Tempest believes collectively indicate that dual antagonism of the EP2 and EP4 PGE2 receptors is an innovative approach to overcome PGE2 immune suppression in human immune cell culture systems in vitro and inhibits tumor development in several mouse tumor models. Additionally, Tempest believes that these results demonstrate that TPST-1495 has significantly increased anti-tumor activity in these experimental systems as compared to single EP4 antagonist molecules.

TPST-1495 Reverses PGE2-Mediated Suppression of Monocyte to Dendritic Cell Differentiation and Activation

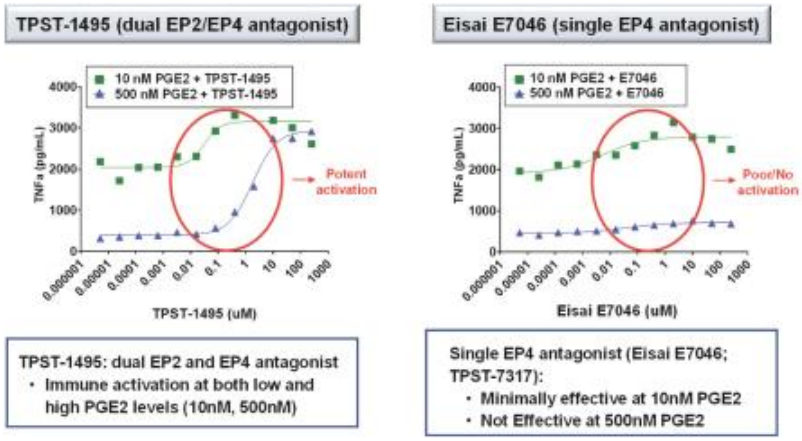
Tempest conducted experiments to evaluate the ability of TPST-1495 to reverse PGE2-mediated suppression of primary human monocyte to dendritic cell differentiation and activation in vitro. Shown in the Figure below, TPST-1495 induced a dose-dependent reversal of PGE2-mediated inhibition of CD1a+/CD16- DC differentiation, with a composite IC50 value for the restoration of DC differentiation under PGE2 suppression of 332 nM (calculated from pooled normalized data from 21 independent experiments; 95% confidence interval 251-439 nM) (Panel A). Cells differentiated in the presence of TPST-1495 also exhibited a dose-dependent increase in expression of CD86+, a co-stimulatory marker known to be expressed on mature activated DCs (Panel B), and a converse effect on expression of CD163+, a marker for immunosuppressive M2 macrophages (Panel C). TPST-1495 also demonstrated a dose-dependent reversal of PGE2-mediated inhibition of the proinflammatory cytokines interleukin (IL)-12p70 and TNFα (see second Figure below). This series of experiments indicates that TPST-1495 targeting both EP2 and EP4 receptors is more potent at overcoming PGE2 immune suppression compared to a single EP4 receptor antagonist.

TPST-1495 Appears to Reverse PGE2-Mediated Immune Suppression in Human Monocytes



Tempest also evaluated the comparative capacity for TPST-1495 and the single EP4 antagonist E7046 (TPST-7317) to reverse prostaglandin-mediated immune suppression in conditions of both high and low PGE2 concentrations in human monocyte cultures in vitro. The literature indicates that plasma PGE2 levels in healthy individuals range from 30 to 336 pM; importantly, PGE2 levels in the TME can be elevated up to 3 nM. However, the actual level in the TME is likely much higher than reported due to the short half-life of PGE2. The rationale for conducting this experiment was to test the capacity of TPST-1495 to reverse immune suppression in a broad range of PGE2 levels that may encompass the range in the TME. Shown in the figure below, in the presence of 500nM PGE2 (blue curves), the observed concentration of TNFα was significantly lower than with 10nM PGE2 (green curves) which is likely due to increased suppression of PGE2 signaling through EP receptors. In both low and high PGE2 conditions, TPST-1495 rescued the production of TNFα by monocytes. In contrast, the single EP4 antagonist E7046 was only able to partially rescue TNFα production when PGE2 concentrations were below the Kd for EP2 (green curve, right graph). When PGE2 concentrations were above the EP2 Kd (blue curve, right graph), the single EP4 antagonist was unable to rescue TNFα production due to the redundancy of inhibition by PGE2 signaling through the EP2 receptor. These results suggest that at appropriate dose levels, TPST-1495 may completely block signaling through both EP2 and EP4 pathways in the TME and that this dual blockade is more effective than EP4 blockade alone to reverse PGE2-mediated immune suppression.

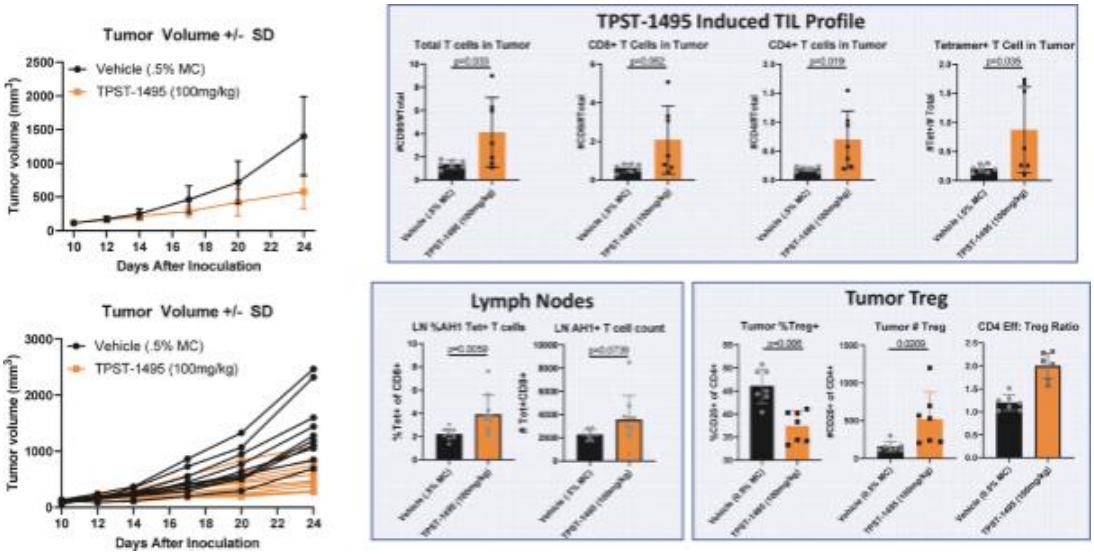
Antagonism of Both EP2 and EP4 Receptors with TPST-1495 is Required to Reverse Immune Suppression in Human Monocytes at High and Low Prostaglandin Levels



TPST-1495 Activity in Mouse Tumor Models

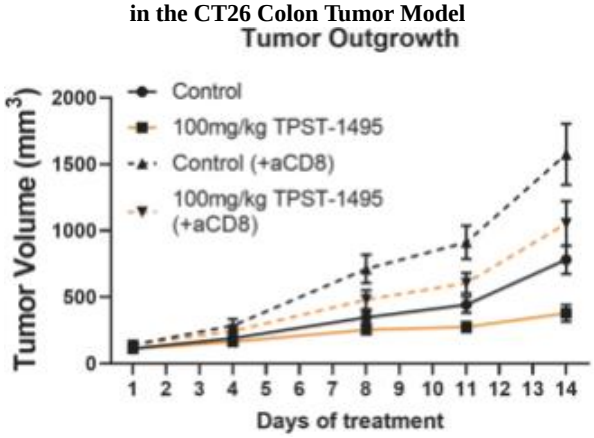
Tempest conducted extensive experiments in several tumor mouse models to evaluate the anti-tumor activity of TPST-1495 and to compare its potency to a single EP4 antagonist E7046, developed by Eisai Co. Ltd., or Eisai. Tempest believes that these experimental results demonstrate that TPST-1495 has increased therapeutic activity in tumor-bearing mouse models and has significantly improved anti-tumor activity compared to single EP4 antagonists. As shown in the figure below, TPST-1495 demonstrated significant efficacy as monotherapy when given to Balb/c mice bearing established flank CT26 colon tumors. In these experiments, Tempest analyzed immune compartments in the TME using flow analysis and immunohistochemistry, or IHC, to evaluate whether the anti-tumor effects observed in this model correlated with changes in tumor-infiltrating lymphocytes, or TILs. Administration of TPST-1495 at 100 mg/kg BID significantly increased the total T cell number and percentage of CD4+ and CD8+ T cells within the tumor compared to vehicle control. Specifically, immunodominant AH1 tumor antigen specific CD8+ T cells (AH1 tetramer+) were significantly elevated ($p = 0.035$). Mice treated with TPST-1495 demonstrated immune activation, with increased effector to Treg cell ratio ($p=0.0001$). Consistent with increased T cells in the TME, the absolute number and frequency of AH1 tetramer+ T cells was also significantly elevated in the tumor draining lymph node.

TPST-1495 Anti-Tumor Response in Mice Correlates with Increased CD8+ T cells and Reduced Tregs in the TME



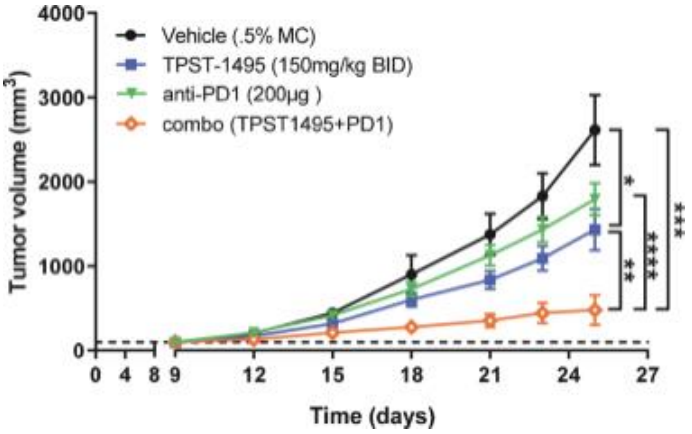
As shown in the figure below, TPST-1495 anti-tumor efficacy in the CT26 colon tumor model was significantly diminished when CD8+ T cells were depleted from the mouse with anti-CD8 antibodies. Additionally, treatment with anti-CD8 antibody reversed the effects of TPST-1495 on tumor infiltration, with a large reduction of CD8+ T cells and AH1 rejection antigen specific CD8+ T cells (data not shown).

CD8+ T cells are Required for the TPST-1495 Mediated Anti-Tumor Response in the CT26 Colon Tumor Model



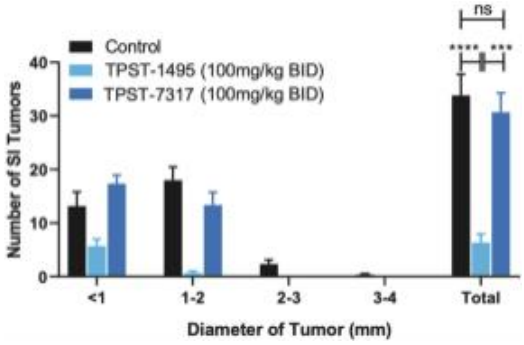
The published literature indicates that blockade of the prostaglandin pathway in mice bearing non-inflamed or “cold” tumors leads to the recruitment of IFNg expressing NK cells, the development of tumor-specific CD8+ T cell immunity and tumor reduction. To support the rationale for combination of TPST-1495 with anti-PD-1 immune checkpoint inhibitors in patients, Tempest tested the possible increased anti-tumor activity in the CT26 model by combining TPST-1495 and anti-PD-1 monoclonal antibody therapies. Shown in the figure below, TPST-1495 alone exhibited a 35% reduction in tumor growth compared to vehicle-treated animals (n = 10 per group). A 31% reduction in tumor growth was observed in mice given anti-PD-1 monotherapy. When combined, TPST-1495 and anti-PD-1 decreased tumor growth by 73%, a significant reduction when compared to either the TPST-1495 ($p = 0.036$) or anti-PD-1 monotherapy cohorts ($p = 0.004$).

TPST-1495 Synergistic Activity with anti-PD1 Combination in CT26 Tumor Bearing Mice



Tempest also evaluated the anti-tumor activity of TPST 1495 in a spontaneous mouse model which recapitulates many aspects of human CRC. The so-named $Apc^{Min/+}$ mice harbor one copy of the multiple intestinal neoplasia (Min) mutant allele of the adenomatous polyposis coli, or(APC, locus and spontaneously develop multiple tumors primarily in the small intestine. Both humans and mice bearing APC mutations are predisposed to the spontaneous formation of adenomas and adenocarcinomas; humans with APC mutations typically develop tumors throughout the small and large intestine. To test the impact of TPST-1495 therapy on small intestine tumor development in the ApcMin/+ model, mice were treated, starting at the age of six weeks, with 100 mg/kg TPST-1495 (n = 12) or methylcellulose (MC) vehicle (n = 12) by twice daily gavage for the duration of eight weeks. The anti-tumor efficacy of dual antagonism of EP2 and EP4 receptors by TPST-1495 was compared to a single EP4-specific receptor antagonist, TPST-7317, which corresponds to E7046, the molecule developed by Eisai and is in clinical development by Adlai Nortye Biopharma. 24, six-week-old ApcMin/+ mice were randomly divided into three groups and treated with methylcellulose vehicle control, or MC, MC-containing TPST-1495 (100 mg/kg) or TPST-7317 (100 mg/kg) by twice-daily gavage for eight weeks. The EP4 antagonist IC50 was comparable for both compounds. As shown in the figure below, TPST-7317 did not significantly inhibit the number and/or size of small intestine tumors (33.83 ± 3.95 tumors in control mice compared to 30.67 ± 3.63 tumors in TPST-7317 treated mice, $p = 0.5683$). In contrast, treatment of mice with TPST-1495 resulted in an approximately five-fold reduction in tumors compared to control mice (6.33 ± 1.65 tumors per small intestine; $p < 0.0001$). Tempest believes that these results demonstrate that TPST-1495 has potent anti-tumor activity as monotherapy and that antagonizing both EP2 and EP4 is significantly more effective at reducing tumor lesions in ApcMin/+ mice compared to single EP4 antagonists.

Dual EP2 and EP4 Antagonism with TPST-1495 has Significantly Increased Anti-Tumor Potency Compared to a Single EP4 Antagonist in the APC Mouse Model of Human CRC



*Significance: * p < 0.05, *** = p < 0.001, **** = p < 0.0001; TPST-7317 is E7046 single EP4 antagonist developed by Eisai*

IND-Enabling Toxicology Studies

The toxicology program for TPST-1495 was designed to evaluate its toxicity profile, enable selection of an appropriate clinical starting dose, and support the oral administration of TPST-1495 to advanced cancer patients. Potential toxicity was characterized in 28-day repeated-dose good-laboratory-practice, or GLP, studies conducted in two relevant species, rats and monkeys.

The primary microscopic target organ in the TPST-1495 toxicology program, common to both species, was the gastrointestinal, or GI, tract. In monkeys, liquid or nonformed feces was noted. Microscopic findings of erosion/ulceration and inflammation in the GI tract were the main observations, which were reversible after a 28-day recovery period. In the rat, the locations of the findings were primarily in the stomach and duodenum, while in the monkey, the locations of findings were the stomach, cecum, and colon.

In the 28-day GLP repeat-dose study conducted in rats, since GI tract microscopic findings were adverse at all doses tested, a no-observed-adverse-effect-level, or NOAEL, was not established. However, the highest non-severely toxic dose, or HNSTD, was 300 mg/kg/day. Clinical pathology findings were limited to animals given ³ 30 mg/kg/day and were consistent with inflammation and blood loss with a regenerative response. Glandular stomach ulcers and/or erosions were observed microscopically in animals at all doses and were associated with inflammatory infiltrates and/or hemorrhage, but the findings were of low incidence and lacked a dose response. Stomach ulcers and erosions were considered adverse at all TPST-1495 doses. At the end of the 28-day drug-free recovery period, there were no ulcers or erosions apparent in animals in any dose group.

In the 28-day GLP repeat-dose study conducted in monkeys, the NOAEL was 100 mg/kg/day. In addition to the GI tract, target organs identified in the monkey included the kidney and liver. Findings in these two organs were only observed at higher doses in initial non-GLP monkey repeat-dose studies. At high doses, moderate to marked increases in urea nitrogen and creatinine were noted, with increased inorganic phosphorus concentrations. Microscopically, kidney findings were characterized as renal tubular degeneration/necrosis, with associated mixed cell inflammation in two animals given 500 mg/kg/day. Clinical chemistry parameters that were increased included total bilirubin, alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Histologic liver findings consisted of hepatocellular hypertrophy, hepatocyte vacuolation, periportal inflammation, and/or Kupffer cell hyperplasia of animals administered ³ 150 mg/kg/day.

TPST-1495 was not mutagenic in a non-GLP bacterial mutation assay, and was found to be not phototoxic in a GLP study conducted in rats.

Ongoing TPST-1495 Phase 1a/1b Clinical study: Overview

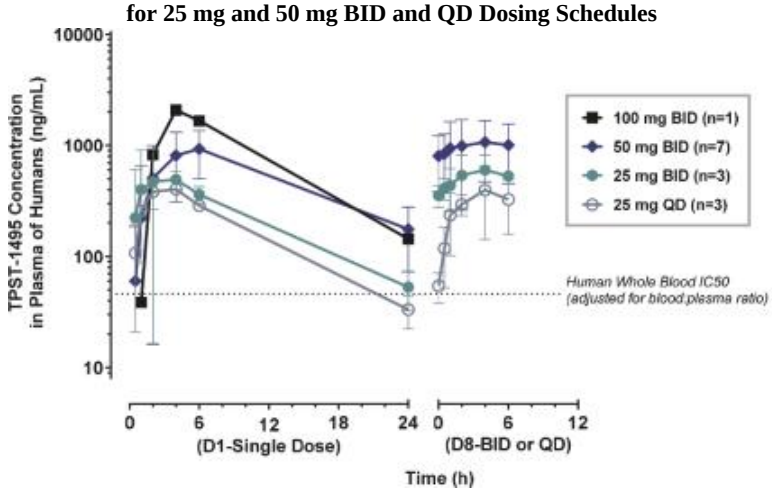
Tempest initiated a first-in-human Phase 1 study in May 2020 to evaluate the safety, tolerability, PK, PD and preliminary anti-tumor activity of TPST-1495 in a multicenter, open-label, dose-escalation, dose and schedule optimization, and expansion study in subjects with advanced solid tumors. Subjects with all histologic types of solid tumors are eligible for the dose-escalation and schedule and dose optimization stages, and to be eligible for study, subjects must have no remaining standard therapy known to confer clinical benefit. The study is composed of three stages. First, the dose-escalation stage will determine the maximum tolerated dose, or MTD, and/or RP2D of single-agent TPST-1495 administered twice daily, or BID. Second, the schedule and dose optimization stage will evaluate alternative TPST-1495 administration schedules and determine a RP2D for the selected schedule. Third, an expansion stage will evaluate the activity of TPST-1495 in targeted patient populations.

The dose escalation stage of the Phase 1a/1b clinical trial was completed in Q1 2021 and patients currently are enrolling in the schedule and dose optimization stage. During the dose escalation stage, TPST-1495 was initially administered on a BID schedule. However, higher than predicted exposure, i.e., greater than IC90 of the EP2 and EP4 receptors at trough exposure, was associated with reduced GI tolerability that limited chronic dosing by subjects on the BID schedule. On the current schedule and dose optimization stage of the trial, TPST-1495 is administered once daily, or QD, and is being evaluated on a continuous dosing and an intermittent dosing schedule of days 1-5, every 7 days. Tempest's hypothesis is that the trough exposure levels achieved with QD dosing will improve gut homeostasis and tolerability for chronic dosing while maintaining the Cmax drug levels that Tempest believes block EP2/EP4 receptor signaling in the TME, thereby providing clinical benefit to subjects during chronic dosing. Both the QD continuous and intermittent administration schedules will be tested at the 25 mg dose level, and possibly higher and lower dose levels.

Overview of Clinical Pharmacology

Pharmacokinetic, or PK, analyses revealed that the drug exposure at steady state in subjects who received the BID dosing schedule remained well above the human whole blood IC50 values for the EP2 and EP4 receptors at 50 mg and 25 mg dose levels. The figure below shows the TPST-1495 concentration-time profiles following a single dose on Day 1 and steady state drug concentrations on Day 8 for the QD or BID dosing schedules. The PK profiles on Days 1 and 8 of study subjects treated at 25 mg on the QD schedule demonstrated that once daily dosing of TPST-1495 reduced the minimum observed plasma concentration, or Cmin, and the steady state exposure levels of drug compared to the BID schedule. Tempest believes that improved exposure on the QD schedule facilitates intestinal mucosal homeostasis and is associated with improved drug tolerability compared to the BID schedule. Based upon the improved drug exposure and tolerability on the QD schedule, we have selected the QD schedule as the preferred schedule for TPST-1495 administration.

Mean Concentration-Time Profiles by Dose Level for TPST-1495 for 25 mg and 50 mg BID and QD Dosing Schedules



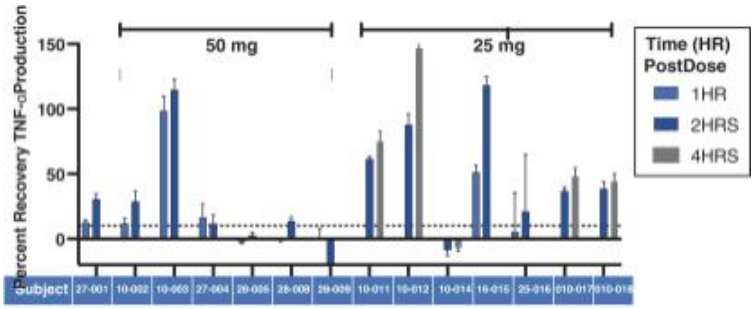
Abbreviations: BID = twice a day; D = day; h = hour; IC50 = half maximal inhibitory concentration.

For BID administration, Day 1 PK is following a single dose, Day 8 is BID, and Day 22 is BID.

Error bars are standard deviations around the mean.

Our pharmacodynamic, or PD, assessment in subjects treated with TPST-1495 includes both the PGE2 whole blood immune suppression assay conducted with patient blood discussed in the nonclinical section and measurements of a stable metabolite of PGE2 known as PGEM in the urine. Shown in the figure below, the first PD results indicate target engagement in subjects dosed with 25 mg TPST-1495, as indicated by the reversal of PGE2 immune suppression in the whole blood assay, as shown by the increase of TNFα production in whole blood monocytes due to TPST-1495 exposure. Tempest has also observed increased levels of PGEM in the urine, resulting from TPST-1495 antagonism of EP2 and EP4 receptors (inferred through measurement of the PGEM metabolite).

Recovery of TNF-a Production in Whole Blood on the First Day Following Dosing with 25 mg and 50 mg TPST-1495



Percent increase of TNF-α measured in subjects' whole blood as indicated by ELISA following stimulation with LPS alone with and without exogenously added PGE2 sampled at the times indicated in the legend post dosing. The values expressed reflect the percent recovery of TNF-α production observed in the presence of PGE2 and TPST-1495 in subject plasma as compared to the level TNF-α production in subject plasma stimulated with LPS alone (without PGE2).

Overview of Preliminary Clinical Safety

As of June 28, 2021, 27 subjects have enrolled into the ongoing TPST-1495-001 study and received at least one dose of TPST-1495 as monotherapy. Enrollment is ongoing and the MTD and/or RP2D are not yet identified. The safety profile of TPST-1495 has been characterized by predominantly (70%) low and moderate Grade 1-2 treatment related adverse events, or TRAE, with 30% of the 27 safety subjects experiencing a Grade 3 TRAE. The most common TRAEs of any grade have been diarrhea (26%), abdominal pain (26%), dyspepsia (22%), anemia (19%), fatigue (19%), and nausea (15%). The only Grade 3 TRAE reported in more than one study subject is anemia (11%). There have been no reported Grade 4 or Grade 5 AEs.

TPST-1495 Treatment-Related Adverse Events

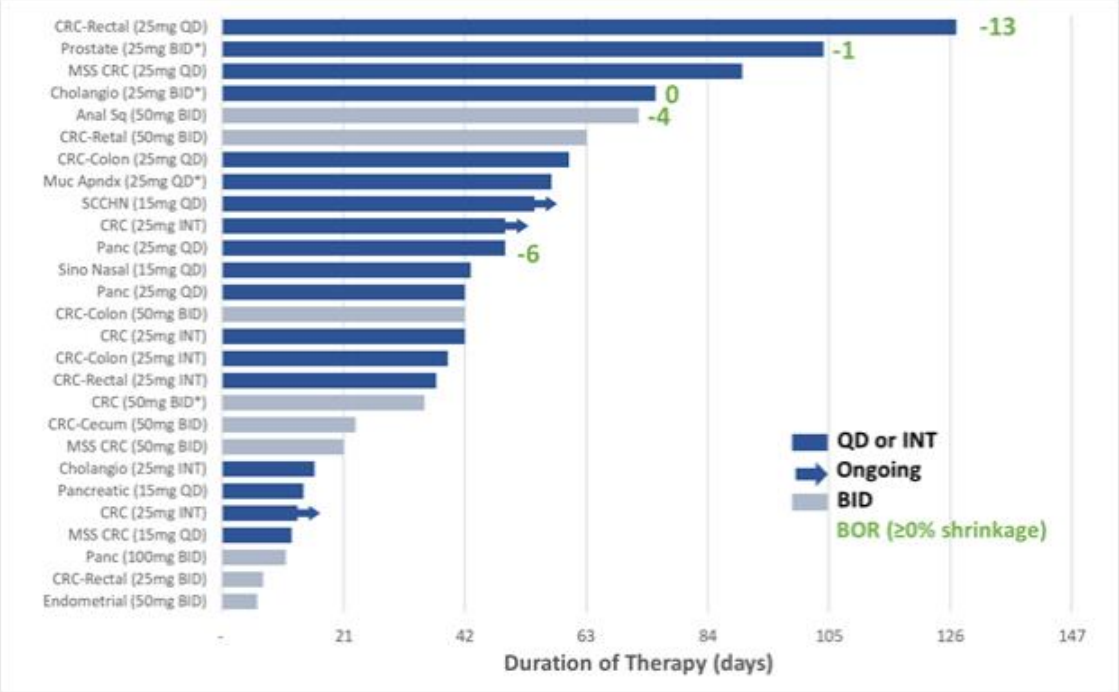
Preferred Term (PT)	All Grades N=27	Grade 3 N=27
Abdominal pain	7 (26%)	
Diarrhea	7 (26%)	1 (4%)
Dyspepsia	6 (22%)	
Anemia	5 (19%)	3 (11%)
Fatigue	5 (19%)	
Nausea	4 (15%)	
Oedema peripheral	3 (11%)	
Vomiting	3 (11%)	

Gastrointestinal hemorrhage	3 (11%)	1 (4%)
Abdominal distension	2 (7%)	
Dizziness	2 (7%)	
Hematochezia	2 (7%)	
Lymphopenia	2 (7%)	1 (4%)
Esophageal hemorrhage	1 (4%)	1 (4%)
Abdominal discomfort	1 (4%)	
Abdominal pain upper	1 (4%)	
Alanine aminotransferase increased	1 (4%)	
Aspartate aminotransferase increased	1 (4%)	
Blood alkaline phosphatase increased	1 (4%)	1 (4%)
Blood creatinine increased	1 (4%)	
Chest pain	1 (4%)	
Chills	1 (4%)	
Colitis	1 (4%)	
Constipation	1 (4%)	
Decreased appetite	1 (4%)	
Dehydration	1 (4%)	
Diverticulitis	1 (4%)	
Duodenal ulcer	1 (4%)	
Dyspnoea	1 (4%)	
Steatorrhea	1 (4%)	
Flatulence	1 (4%)	
Gastric ulcer	1 (4%)	
Gastrointestinal pain	1 (4%)	
Gastrooesophageal reflux disease	1 (4%)	
Hemoglobin decreased	1 (4%)	
Melaena	1 (4%)	
Mucosal Inflammation	1 (4%)	
Neutropenia	1 (4%)	
Pruritus	1 (4%)	
Pyrexia	1 (4%)	
Rash maculo-papular	1 (4%)	
Rash pruritic	1 (4%)	
Renal pain	1 (4%)	
Thrombocytopenia	1 (4%)	
Tumor pain	1 (4%)	

Overview of Preliminary Clinical Activity

As of June 28, 2021, 27 subjects have enrolled into the study and received at least one dose of TPST-1495 as monotherapy treatment. The Swimmer's plot shown below summarizes the TPST-1495 treatment duration (in some cases ongoing) of all dosed patients in this intent-to-treat population and is annotated with the Best Overall Response, or BOR, for subjects who achieved 0% tumor growth or reduction of target lesions on treatment. Of note, these emerging data indicate that subjects starting on (or reduced to) the QD schedule at the current 25 mg dose have a generally increased duration of treatment and improved objective tumor response compared to the BID schedule, consistent with improved tolerability and more prolonged dosing with the QD schedule. In addition, four patients on the 25 mg QD dose schedule experienced a reduction in disease specific tumor marker, i.e., PSA and CEA in prostate and colon cancer subjects respectively. With 1 subject ongoing before first tumor assessment, a best response of stable disease, or SD, has been observed in 35% (9/26) of study subjects treated to date, including shrinkage of measurable disease up to -13%. Enrollment into the dose and schedule optimization cohorts continues with identification of the monotherapy RP2D anticipated by the end of 2021 or in early 2022.

TPST-1495 Treatment Duration and Best Overall Response



* *Asterisk denotes a dose reduction during course of study; asterisked 25mg BID patients changed schedule to 25mg QD. Data source are electronic data capture and site clinical site communications and are preliminary partially-unmonitored data. For ongoing patients, last dose of TPST-1495 assumed to be June 28, 2021. Subjects shown in the Figure were enrolled into the Dose Escalation or the schedule and dose optimization arms of the Phase 1a/1b clinical study.*

Overview of TPST-1495 Next Steps

Once the TPST-1495 monotherapy RP2D and schedule are identified, Tempest plans to initiate focused expansion cohorts to evaluate monotherapy TPST-1495 in (i) specific patient populations that are strongly associated with prostaglandin signaling and high expression of EP2 and EP4 receptors, and (ii) a biomarker-defined basket cohort limited to patients with an activating mutation in a gene associated with anti-tumor benefit from inhibition of prostaglandin signaling in both preclinical and clinical studies. Additionally, in the second half of 2021, Tempest plans to initiate the evaluation of TPST-1495 in combination with anti-PD-1 therapy based upon the strong preclinical evidence generated by Tempest that TPST-1495 reduces the immune suppressor cell population and increases immune effector cells in the tumor microenvironment, as well as the strong combinatorial activity of TPST-1495 and anti-PD-1 therapy in immune competent *in vivo* preclinical models.

TPST-1120: PPARα Transcription Factor Antagonist

Overall Program Summary

TPST-1120 is potentially a first-in-class oral, small molecule antagonist of Peroxisome Proliferator-Activated Receptor-alpha, or PPARα, currently in multicenter, open-label, dose-escalation, Phase 1a/1b clinical studies as both monotherapy and in combination with nivolumab in patients with advanced solid tumors. The dose escalation phase of the clinical study has been completed, and the combination arm is ongoing. Tempest has observed evidence of TPST-1120 clinical activity in the dose escalation arms, and plans to disclose the results of the monotherapy and combination therapy dose escalation studies in the first half of 2021. Tempest expects to initiate a multicenter global randomized Phase 1b/2 clinical study in collaboration with Hoffman-La Roche Ltd. in the mid 2021 that will evaluate TPST-1120 in combination with atezolizumab (Tecentriq®) and bevacizumab (Avastin®) in previously untreated patients with advanced hepatocellular carcinoma, or HCC.

As illustrated in the figure below, tumors evolve to modulate metabolism to promote their own survival, promote angiogenesis and to evade immune recognition. PPARα is a transcription factor that is activated through binding of long-chain fatty acid ligands, which in turn regulates the expression of >100 genes that control glucose and lipid homeostasis, inflammation, proliferation, differentiation and cell death. Included among these regulated genes are those that enable FAO and b-oxidation metabolic pathways in cellular peroxisomes and in mitochondria. An FAO metabolic profile is associated with tumor proliferation, induction of angiogenesis and immune suppression. Published studies and internal Tempest analyses of over 9,000 primary or metastatic tumor samples in the TCGA public database reveal a metabolic gene expression profile characterized by increased PPARα, FAO genes and lipogenesis associated with increased metastatic potential and reduced survival enrichment among multiple cancers, including HCC, cholangiocarcinoma, breast carcinoma, colorectal adenocarcinoma, RCC, lung adenocarcinoma, and prostate adenocarcinoma. TPST-1120 is designed to collectively block the pathways that support tumor cell proliferation, angiogenesis and immune suppression, resulting in reduced disease and patient benefit.

TPST-1120 Mechanism of Action

Rationale for Clinical Evaluation of TPST-1120 in Solid Tumors: The Role of PPARα in Cancer

Peroxisome Proliferator-Activated Receptors, or PPARs, are ligand-activated transcription factors involved in the regulation of glucose and lipid metabolism homeostasis, inflammation, proliferation, differentiation and cell death. The three PPAR subtypes, PPARα, PPARg and PPARb/d, are activated in tumors, where they appear to modulate cell proliferation, differentiation and survival, supporting an important role of PPARs in cancer biology. PPARα regulates the expression of about 100 genes, including those that produce enzymes that enable metabolic processes in cellular peroxisomes and mitochondria known as fatty acid oxidation, or FAO, or ß-oxidation. PPARα expression levels and FAO metabolism is increased in selected healthy, including liver, heart, skeletal muscle, brown adipose tissue, and kidney.

It has been published that multiple human hematologic and solid tumor malignancies demonstrate comparatively increased expression levels of the PPARα transcription factor, its activating ligands including long-chain fatty acids, and PPARα induced genes. This metabolic profile has been observed in hypoxic metastases and extends to immune suppressor cell populations that include myeloid- and lymphoid-derived effector cell populations in the tumor microenvironment, such as dendritic cells and CD8+ T cells which are rendered non-functional, or exhausted, by virtue of utilizing FAO. These published findings indicate that the FAO metabolic pathway enables both tumor cell proliferation and evasion of tumor-specific immune recognition. Tempest interrogated the TCGA public data base to determine which human cancers expressed the highest levels of PPARα and 30 of its targeted genes. Interestingly, Tempest found that FAO is a favored metabolic pathway in HCC, cholangiocarcinoma, breast carcinoma, colorectal adenocarcinoma, RCC, lung adenocarcinoma, and prostate adenocarcinoma. This analysis has served as a primary rationale along with the published literature to guide Tempest's TPST-1120 initial clinical strategy.

In support of Tempest's clinical strategy to evaluate TPST-1120 in patients with HCC, it has been shown in published preclinical studies that therapeutic benefit is observed in mice bearing activated b-catenin pathway liver tumors—also common in human HCC—given a small molecule drug known as etomoxir which targets an FAO pathway protein known as CPT1. In a separate line of investigations, PPARα-deficient mice have been shown to be refractory to the liver carcinogenic effects of an activated ß-catenin pathway or by treatment with the PPARα fibrate agonist WY14643, which is carcinogenic in wild-type mice. The foundational scientific rationale for targeting PPARα with an antagonist was demonstrated in a published study describing a series of experiments conducted in PPARα deficient mice. When these mice were implanted with tumors—which also lacked a functional PPARα gene—the tumors initially established, grew, but then spontaneously completely regressed, due to an inability to convert to FAO metabolism to support continued tumor proliferation. These reports and others support the scientific rationale for targeting the PPARα for the treatment of cancer. Although there have been a few PPARα antagonists that have exerted beneficial effects in preclinical cancer models, to date, no selective PPARα antagonists have been tested in human trials.

Summary of TPST-1120 Preclinical Results

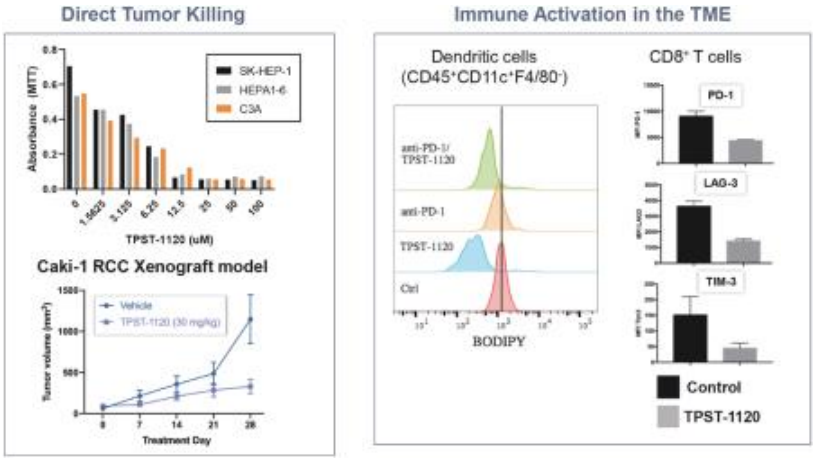
Tempest has conducted pre-clinical pharmacology studies along with PK and toxicology studies with TPST-1120 to support its ongoing evaluation for the treatment of patients with advanced solid tumors. The combined results of the preclinical studies that Tempest has performed indicate that the TPST-1120 anti-tumor response mechanism of action involves both directly inhibiting tumor proliferation and targeting suppressive immune response pathways to promote effective tumor-specific immunity. Tempest's preclinical results support the large body of published literature that the PPARα target genes play an integral role in tumor growth, angiogenesis and evasion of immune recognition and provide the scientific rationale for targeting this pathway with TPST-1120.

Specifically, TPST-1120 has shown the following properties in nonclinical studies:

- Potent human PPARα binding (time-resolved fluorescence resonance energy transfer [TR-Fret] reporter EC50 = 0.011 μM)
- Potent human PPARα inhibition (luciferase reporter IC50 = 0.052 μM)
- Direct and dose-dependent inhibition of cultured primary tumor cells from 14 patients with chronic lymphocytic leukemia
- Promotion of macrophage repolarization (increase in M1/M2 ratio) in PancOH7 syngeneic tumor model
- Therapeutic benefit of TPST-1120 in syngeneic mouse MC38 colorectal cancer model in parental C57BL/6 mice, but not in Goldenticket (STING-/-) or in BatF3 gene knockout mice, indicating an immunomodulatory mechanism, operating through Stimulator of INterferon Genes (STING) and CD8α dendritic cells
- Restoration of thrombospondin-1 (TSP-1) to homeostatic levels in B16F10 and PancOH7 models, suggesting TSP-1 plays a role in TPST-1120 anti-tumor activity. TSP-1 has been shown to be a potent endogenous inhibitor of angiogenesis
- Inhibition of growth of melanoma (B16F10), colon (MC38) and Lewis lung syngeneic carcinoma models with TPST-1120 monotherapy at a dose of 30 mg/kg twice daily
- Significant synergistic inhibition of growth of syngeneic mouse MC38 colorectal and ID8 ovarian cancer models in combination with anti-programmed cell death protein 1 (PD-1)
- Induction of anti-tumor immune memory in an orthotopic ID8 ovarian and syngeneic MC38 colorectal cancer models when combined with anti-PD-1
- Synergistic response with chemotherapies including gemcitabine in PancOH7 model and paclitaxel in Lewis lung carcinoma

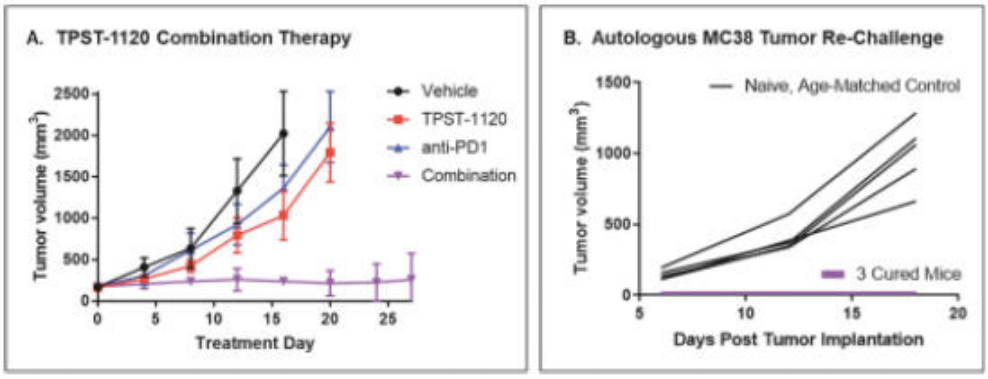
The figure below shows experimental results that are illustrative of the TPST-1120 dual mechanism of action, or MOA, targeting both tumor cells and suppressive immune cell populations. The left upper panel demonstrates that TPST-1120 can directly kill three different HCC human tumor cell lines in vitro in a dose-dependent fashion, consistent with Tempest's findings from the Human Cancer Genome, or TCGA, database that HCC had the highest level of PPARα-induced genes of all malignancies. Tempest's TCGA analysis also demonstrated that renal cell cancer, or RCC, is an FAO-reliant malignancy. Shown in the lower left panel in the figure below, TPST-1120 monotherapy inhibited tumor growth in immune deficient mice implanted with Caki-1 human RCC tumor cells. The experimental results shown in the right panel below were conducted in C57BL/6 mice bearing syngeneic MC38 colon tumors and treated TPST-1120. Tempest analyzed two immune cell populations in the MC38 TME to test whether TPST-1120 therapy inhibited suppressive or non-functional immune cell populations. Using BODIPY flow cytometry, which is a method to measure cellular uptake of long chain fatty acids, Tempest found that TPST-1120 therapy inhibited uptake of the PPARα transcription factor activating ligand in toleragenic dendritic cells, thus inhibiting the preferred metabolic pathway of this suppressive immune cell population. Shown in the right panel of the Figure, TPST-1120 treatment of MC38 tumor-bearing mice also reduced the expression of PD-1, LAG-3 and TIM-3 exhaustion markers on tumor infiltrating CD8+ T cells.

TPST-1120 Directly Inhibits Tumor Cell Proliferation and Immune Suppression in the TME



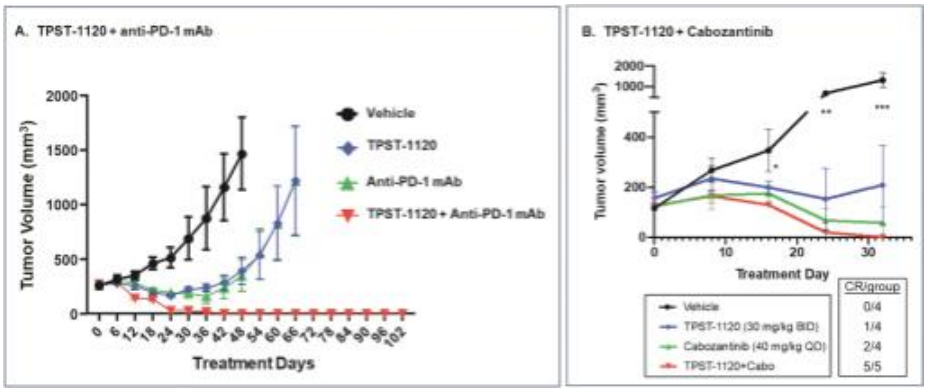
Immune checkpoint blockade enhances anti-tumor immunity by restoring the activity of cytotoxic T (Teff) cells. Emerging experimental results suggest that inhibiting FAO with a PPARα antagonist may target resistance mechanisms to both anti-PD-L1/PD-1 and anti-VEGF therapies. Upon ligation between PD-1 on tumor-infiltrating T cells with PD-L1 expressed on tumor cells, metabolic T-cell re-programming occurs, which is characterized by a shift from glycolysis to FAO, thereby restricting T-effector cell differentiation and promoting suppressive T-regulatory cells. The rationale for targeting PPARα is to inhibit suppressive immune cells in the tumor microenvironment and promote the function and/or recruitment of cytotoxic T effector cells, thus enhancing the efficacy of anti-PD-L1 blockade. In this context, inhibiting FAO metabolism has the combined effect of inhibiting tumor cell growth directly and also the metabolism of suppressive immune cell populations, markedly improving the success of immunotherapies. These observations support both the scientific rationale and provide insights into clinical evaluation of combining TPST-1120 with PD-(L)-1 immune checkpoint inhibitor antibodies. Shown in panel A in the figure below, while both TPST-1120 or anti-PD-1 monotherapy inhibited outgrowth of established flank MC38 tumors, the combination of these two agents resulted in synergistic anti-tumor activity. Shown in panel B, MC38 tumor-bearing mice cured by the combination therapy, unlike age-matched naïve control mice, were completely refractory to tumor growth when rechallenged with autologous MC38 tumor cells. These results demonstrate that TPST-1120 in combination with anti-PD-1 induced lasting tumor-specific immune memory.

Significant Anti-Tumor Activity and Induction of Tumor-Specific Immune Memory is Observed in MC38 Colon Tumor Bearing Mice Given with TPST-1120 + anti-PD-1 mAb Combination Therapy



PPARα orchestrates the metabolic re-programming to utilize FAO as the main energy source in mice with ß-catenin-activated HCC. PPARα deficient mice are refractory to the liver carcinogenic effects of the activated ß-catenin pathway and the PPARα fenofibrate agonist WY14643. Since a significant proportion (up to 50%) of HCC cancers have Wnt-ß-catenin pathway activation, Tempest tested the activity of TPST-1120 in the Hepa 1-6 tumor cells, which are a syngeneic ß-catenin driven HCC tumor. Shown in panel A of the figure below, Tempest observed a synergistic reduction in established tumor volume and long-term durable cures when TPST-1120 therapy was combined with an anti-PD-1 antibody. Additionally, tumor resistance to anti-angiogenic drugs is associated with elevated lipogenesis and FAO, primarily through the vascular regression and hypoxic environment that this class of therapies engenders. In response, tumor cells can switch to FAO as a mechanism of resistance against anti-angiogenic therapy. The published literature indicates that in the MC38 CRC model, inhibiting FAO is highly effective in overcoming this resistance when administered in combination with anti-VEGF therapy. Tempest confirmed that combination of TPST-1120 with anti-angiogenesis therapy confers potent anti-tumor activity. Shown in panel B of the Figure below, Tempest's preliminary results show complete reduction of established MC38 tumors in mice given a combined therapy of TPST-1120 with the approved VEGF receptor tyrosine kinase inhibitor cabozantinib. Taken together, the experimental results shown in this Figure provide the scientific rationale for the planned clinical evaluation of TPST-1120 therapy in front-line HCC in combination with atezolizumab and bevacizumab, and evaluation of TPST-1120 in combination with cabozantinib in FAO-reliant malignancies such as HCC and RCC.

Anti-Tumor Activity of TPST-1120 Combination Therapy with Immune Checkpoint or Angiogenesis Inhibitors



IND-Enabling Toxicology Studies

The toxicology program for TPST-1120 was designed to evaluate its toxicity profile, enable selection of an appropriate clinical starting dose, and support the oral administration of TPST-1120 to advanced cancer patients. Potential toxicity was characterized in 28-day repeated-dose good-laboratory-practice (GLP) studies conducted in two relevant species, rats and dogs. In the GLP study conducted in rats, audible respiration with labored respiration caused the early sacrifice of one rat at 1000 mg/kg/day. A similar finding had been noted in a non-GLP 14-day repeated-dose study, where there were five deaths and wheezing was reported as a clinical sign at 1000 mg/kg/day. There was no pathologic cause of death for this finding. In the GLP study, a dose of 750 mg/kg/day was considered to be the severely toxic dose in 10% of animals (STD10), while the no-observed-adverse-effect level (NOAEL) was 250 mg/kg/day

In the 28-day GLP repeat-dose toxicity study conducted in dogs, the highest non-severely toxic dose (HNSTD) was 1000 mg/kg/day due to the lack of severely toxic findings at that dose. The NOAEL in dogs was 300 mg/kg/day. The two primary microscopic target organs identified in both species were the liver and kidney. The findings were different in the two species and were adverse in dogs at the high dose of 1000 mg/kg/day. Conversely, microscopic findings were not found to be adverse in rats. The third target organ based on clinical signs, which was also common to both species, was the GI tract.

TPST-1120 was not mutagenic in a non-GLP bacterial mutation assay and was not found to be phototoxic in a GLP study conducted in rats.

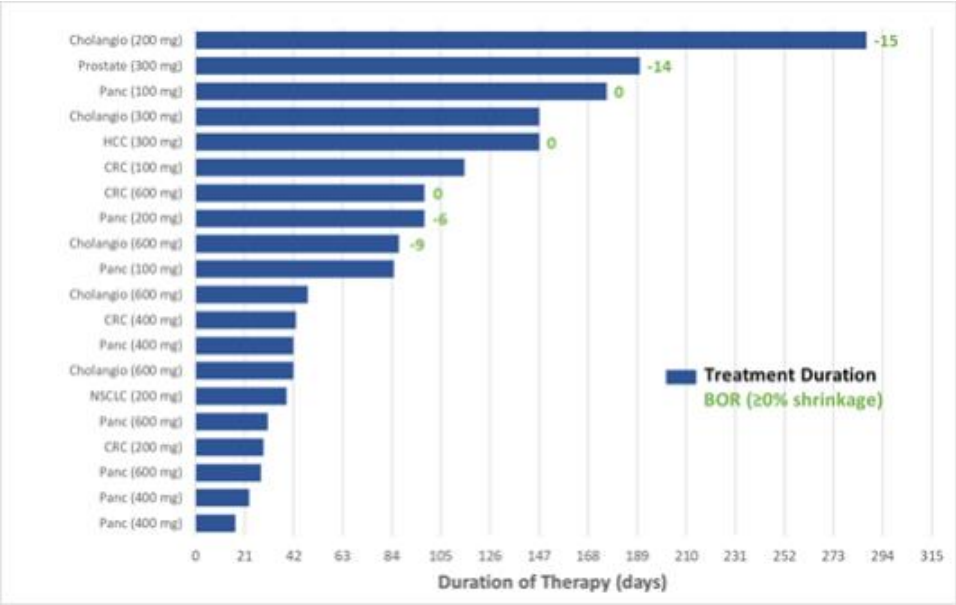
Ongoing TPST-1120 Phase 1a/1b Clinical study: Overview, Status & Safety

Tempest is sponsoring an ongoing, first-in-human, open-label, dose-escalation and dose-expansion Phase 1/1b study evaluating the safety, pharmacokinetics, pharmacodynamics, and preliminary efficacy of TPST-1120 alone and in combination with systemic anti-cancer therapies in patients with advanced solid tumors. Part 1 of the study is designed to determine the MTD and/or RP2D of TPST-1120 monotherapy. Part 2 is designed to determine the MTD and/or RP2D of TPST-1120 in combination with the anti-PD-1 monoclonal antibody, nivolumab. Parts 3 and 4 (not open) are designed to evaluate the anti-tumor activity of TPST-1120 monotherapy and in combination with nivolumab at the MTD or RP2D in tumor-specific expansion cohorts, respectively.

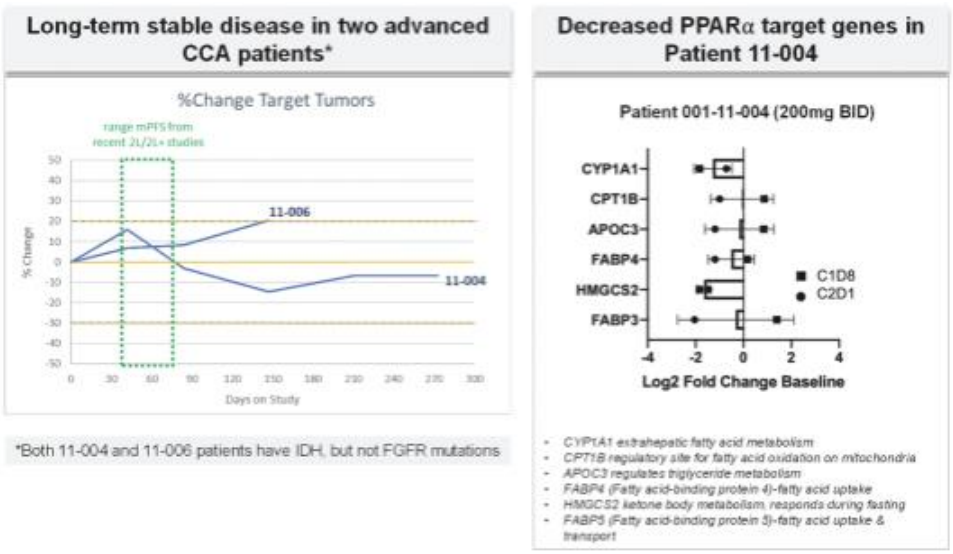
As of a data cutoff date of June 28, 2021, 20 subjects have been dosed on the Phase 1 study with TPST-1120 at escalating doses from 100 mg BID to 600 mg BID. No DLTs have been reported and the MTD not reached at the highest dose level tested. The RP2D of monotherapy TPST-1120 for further development is 600 mg BID. The majority of TPST-1120 related adverse events, including at the 600 mg BID dose, have been Grade 1-2 in severity and manageable without requiring dose hold or dose reduction. The most common related adverse events reported have been nausea, fatigue, and diarrhea, all £ Grade 2 in severity. Only one Grade 3 related adverse event (Grade 3 hypertension) considered by the investigator to be possibly/probably related to TPST-1120 has been reported, and no > Grade 3 AEs have been reported. No subjects have had TPST-1120 discontinued due to a drug-related toxicity. In the preliminary combination cohorts with nivolumab, 11 subjects have been dosed with escalating doses of TPST-1120 from 100 mg BID to 400 mg BID and the dose escalation continues with the highest dose to be tested being the monotherapy RP2D of 600 mg BID. No DLTs have been reported for the combination regimen to the data cut-off date, and the safety profile of the combination appears consistent with the individual profiles of the two drugs. Pharmacokinetic analysis of TPST-1120 in study subjects has demonstrated dose-proportional exposure with increasing dose up to the highest dosed level tested. Additionally, pharmacodynamic (PD) assessment of on-target activity in patients has demonstrated modulation of triglycerides and PPARα controlled gene expression in TPST-1120 treated subjects.

While the primary objective of the dose escalation is to characterize the TPST-1120 safety profile and determine the recommended dose for development, Tempest is encouraged by the observations of prolonged disease control in some patients as well as RECIST stable disease with tumor shrinkage (up to -15%) achieved with monotherapy TPST-1120 during the dose escalation stage. Extended time on study has occurred in subjects with late-line treatment refractory cancers, including cholangiocarcinoma which is known to have particularly short time-to-progression with standard-of-care in the late-line treatment setting. Shown below, one subject with late line cholangiocarcinoma had a 15% tumor shrinkage and was on study for over nine months of treatment while also demonstrating on-target inhibition of expression of PPARα target genes on PD assessment.

TPST-1120 Monotherapy Treatment Duration and Best Overall Response



Long-Term Tumor Control and PPARα Target Gene Modulation in Late-Line Cholangiocarcinoma Patients Treated with TPST-1120 Monotherapy

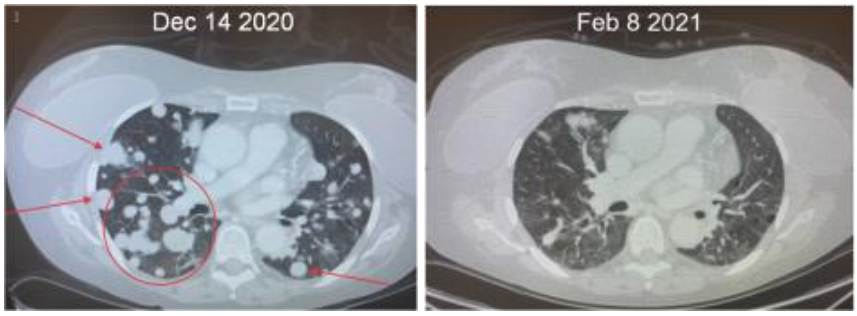


The dose escalation of TPST-1120 in combination with nivolumab is continuing and has not reached a MTD or RP2D. However, Tempest is encouraged by preliminary signs of activity with a deep RECIST partial response (PR) with an overall reduction of -61% in tumor burden observed in a subject with 4th line RCC who had already progressed on the combination of nivolumab and ipilimumab. Shown below, this subject had extensive metastatic disease at study entry including large-burden pulmonary metastases, multiple soft tissue metastases and bone metastases. Her prior therapies included (best response and reason for discontinuation):

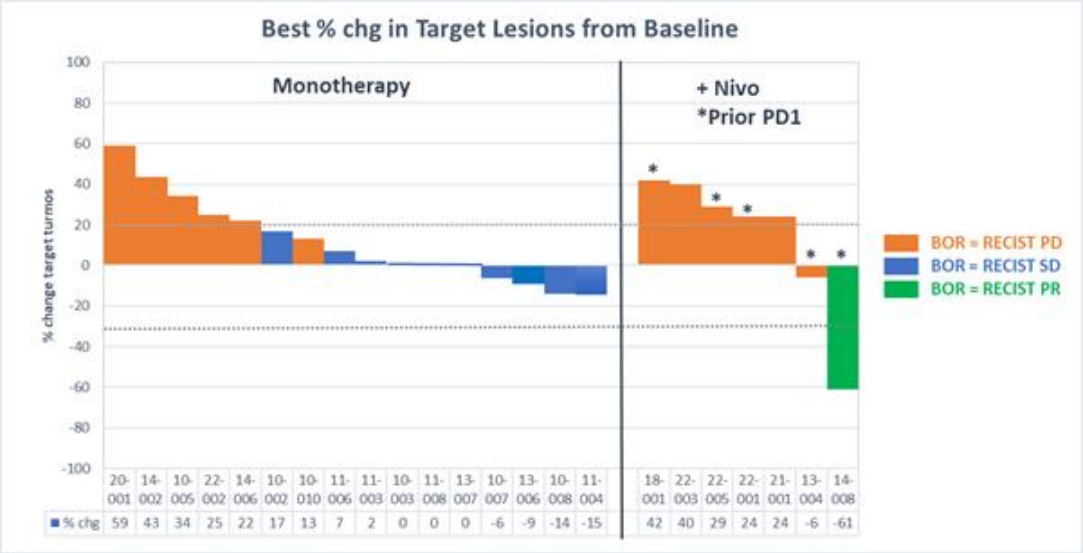
- First-line: ipilimumab + nivolumab (SD, PD)
- Second-line: cabozantinib (SD, PD)
- Third-line: everolimus (SD, PD)

Notably, this subject had been treated with the combination of nivolumab and ipilimumab without experiencing an objective response and then had experienced progression of cancer on this IO doublet, followed by progression of cancer on both cabozantinib and everolimus before initiating treatment with TPST-1120 and nivolumab. The initial RECIST PR (-54%) was seen at the first on-study assessment at eight weeks and included a response in all target lesions as well as complete radiographic resolution of multiple sites of metastatic disease (see CT scan), and was confirmed in second and third on-study assessments at 16 and 24 weeks, respectively, and had deepened to a 61% reduction. Tempest feels that induction of an objective response despite resistance to nivolumab could reflect either monotherapy activity of TPST-1120 on an FAO-dependent tumor or, based upon the mechanism of action and the extensive supporting pre-clinical data, reduction of immune suppressive cells and release of the subject's own anti-cancer immune response.

Partial Response in Late-Line RCC Patient Treated with TPST-1120 and Nivolumab Combination Therapy



TPST-1120 Monotherapy and Nivolumab Combination Therapy Waterfall Plot



Planned TPST-1120 Phase 1b/2 Clinical study in Front Line HCC

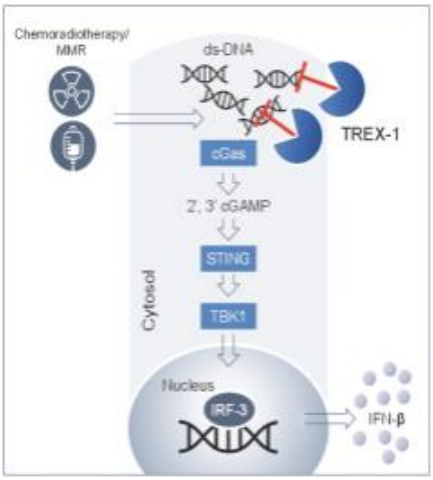
Based upon the TPST-1120 mechanism of action, preclinical data demonstrating synergy with both anti-PD-1 and anti-angiogenesis agents, together with the encouraging safety profile and early signs of anti-tumor activity, Tempest and Roche entered into a clinical collaboration with Roche to evaluate TPST-1120 in combination with atezolizumab and bevacizumab in patients with advanced/metastatic HCC not-previously treated with systemic therapy. This global, randomized, open-label, Phase 1b/2 trial will be operationalized by Roche and will evaluate the triplet regimen of TPST-1120 + atezolizumab + bevacizumab randomized against the standard-of-care doublet of atezolizumab + bevacizumab in the first-line systemic treatment of patients with HCC. The primary objective of this study is to evaluate the anti-tumor efficacy of the combination as determined by confirmed ORR by RECIST 1.1. Additional efficacy endpoints include progression free survival, or PFS, overall survival. or OS, and duration of response, or DOR, while a key exploratory objective is to identify biomarkers that are predictive of response to the experimental treatment, including an assessment activation of the ß-catenin pathway, which is predicted to be present in approximately 50% of patients with HCC. Tempest anticipates that enrollment to this clinical collaboration will initiate in mid-2021.

TREX-1 Inhibitor Program

Tempest believes that the exonuclease TREX-1 may be the optimal approach to drug the STING pathway (**ST**imulator of **IN**terferon **G**enes) with an orally available small molecule inhibitor. Extensive genetic evidence from human disease that has been confirmed in numerous mouse genetic knock-out investigations point to the STING pathway as a critical innate immune sensor for the development of immunity. Although the STING pathway has significant scientific validation, the clinical trials sponsored by several groups utilizing intratumoral delivery of synthetic cyclic dinucleotide STING agonists have been somewhat disappointing. The underlying scientific hypothesis for these clinical trials was that localized T cell priming in the lymph nodes draining from the injected tumor would have activity against non-injected distal tumors, sometimes referred to as the abscopal effect. It is well-known that metastatic tumors have unique antigenic repertoires, indicating a need for global innate activation in the TME of all metastases in order to prime T cells that can recognize and broadly eradicate distinct tumors. However, it may be difficult to achieve a therapeutic index with systemically delivered STING agonists due to the ubiquitous expression of this central innate immune receptor.

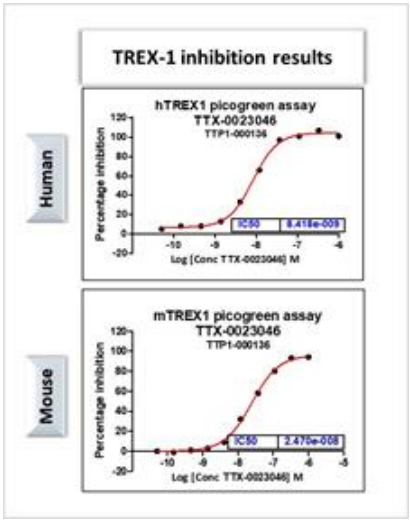
Shown in the Figure below, TREX-1 is a cytosolic exonuclease that inhibits activation of the cGAS/STING pathway by degrading double-stranded (ds) DNA. Genetic instability, DNA repair mutation, and selected therapeutic interventions such as DNA-modifying chemotherapeutic agents or radiation cause TREX-1 expression to increase across diverse malignancies. The increased expression of TREX-1 in tumors serves as the foundational scientific evidence that tumors can hijack this pathway to prevent activation of the STING pathway and avoid immune recognition. The underlying scientific hypothesis for the program is that systemic oral dosing with a potent and specific inhibitor will activate the STING pathway selectively in the TME and prime cytolytic CD8+ T cells broadly in tumor draining lymph nodes serving distinct metastatic lesions having unique antigenic repertoires.

TREX-1 DNA Exonuclease Modulates cGAS/STING Pathway and Innate Immunity



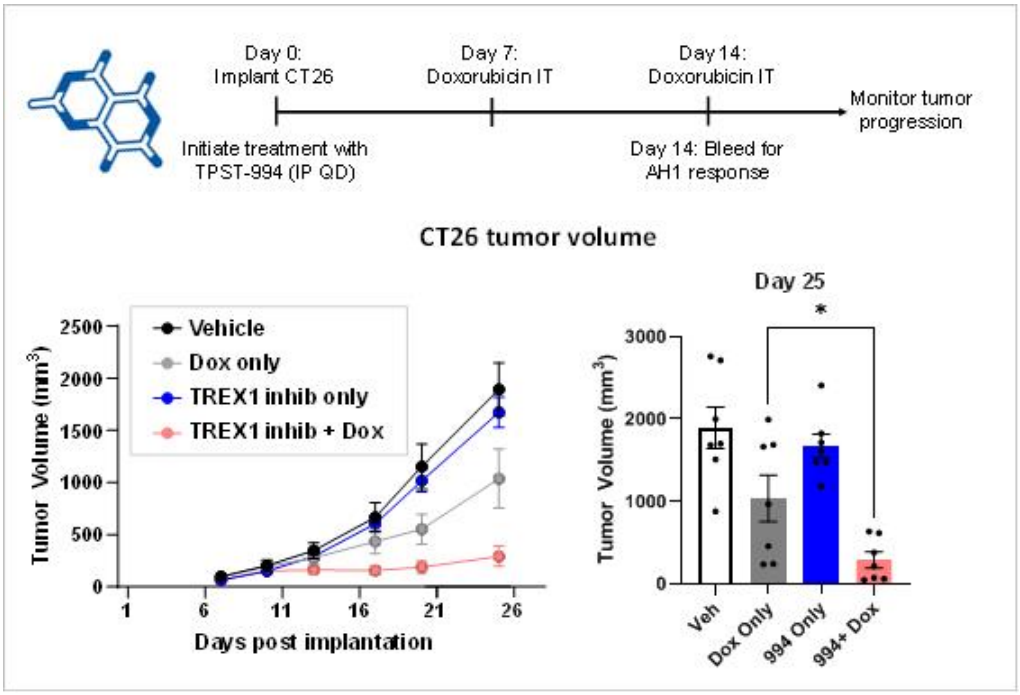
Tempest is currently advancing a lead series with a >1000-fold increase in structure-activity-relationship, or SAR, with an IC50 inhibitory value as low as 8 nM in human TREX-1 inhibitor biochemical assays. As shown by the figure below, the lead series is also active against mouse TREX-1, which we believe will facilitate development and IND-enabling studies once we select a development candidate.

Lead Series Compound-Mediated Inhibition of TREX1 Activity in Biochemical Assay



The foundational scientific rationale for targeting TREX-1 as an approach to selectively activate STING in the TME is predicated upon findings that TREX-1 expression itself is increased in tumor cells due to elevated levels of cytosolic DNA resulting from genetic instability, DNA repair mutation or particular therapeutic interventions such as DNA-modifying chemotherapeutic agents or radiation. Increased TREX-1 expression results in reduction of cytosolic DNA, diminished activation of the cGAS/STING pathway and reduced anti-tumor immunity. To demonstrate proof-of-concept for our novel approach, we initiated a once daily regimen of intraperitoneal injection (to achieve systemic delivery) of Balb/C mice with a TREX-1 inhibitor compound from our lead compound series. On the same day of initiating therapy, mice were given a subcutaneous flank injection of syngeneic CT26 tumor cells. Subtherapeutic doses of doxorubicin, or dox, were given by intratumoral injection on days 7 and 14 post tumor cell implantation as a mechanism to induce DNA damage and induce TREX-1 expression. As shown in the figure below, CT26 tumor outgrowth was significantly ($p \leq 0.5$) diminished only in mice (n = 7) that were given both dox and the TREX-1 inhibitor. We believe these results provide proof-of concept evidence for TREX-1 inhibitor-dependent anti-tumor efficacy.

Lead Series TREX-1 Inhibitor Reduces Tumor Outgrowth



License agreements

In February 2021, Tempest entered into a collaboration agreement with Roche to accelerate the development of TPST-1120 into a frontline, randomized study. Under the terms of the collaboration agreement, Roche will evaluate TPST-1120 in a global randomized phase 1b/2 clinical study in combination with the standard-of-care first-line regimen of atezolizumab and bevacizumab in patients with advanced or metastatic HCCnot previously treated with systemic therapy. Pursuant to the terms of the collaboration agreement, Roche will manage the study operations for the trial and Tempest will supply TPST-1120 for the study and will retain global development and commercialization rights to TPST-1120. All rights to invention and discoveries relating solely to TPST-1120 or biomarkers solely related to TPST-1120 made during any study will be the exclusive property of Tempest. All data generated in the performance of any study under the collaboration agreement will be the property of Roche, but Tempest is entitled to use the data for any lawful purpose.

The collaboration agreement is effective from February 23, 2021 and continues to be in force on a study-by-study basis until the last treatment of the last patient in a study receiving TPST-1120 in accordance with the protocol for such study or until the termination of the collaboration agreement by either party. Upon any termination of the agreement, neither Tempest nor Roche will be entitled to any compensation, damages or other payment.

Sales and marketing

Tempest intends to retain significant development and commercial rights to its product candidates and, if marketing approval is obtained, to commercialize its product candidates on its own, or potentially with a partner, in the United States and other regions. Tempest currently has no sales, marketing or commercial product distribution capabilities. Tempest intends to build the necessary infrastructure and capabilities over time for the United States, and potentially other regions, following further advancement of its product candidates. Clinical data, the size of the addressable patient population, the size of the commercial infrastructure and manufacturing needs may all influence or alter its commercialization plans. If Tempest builds a commercial infrastructure to support marketing in North America, such commercial infrastructure could be expected to include a targeted sales force supported by sales management, internal sales support, an internal marketing group and distribution support. To develop the appropriate commercial infrastructure internally, Tempest would have to invest financial and management resources, some of which would have to be deployed prior to any confirmation that one of its product candidate will be approved.

Manufacturing

Tempest does not own or operate, and currently has no plans to establish, any manufacturing facilities. Tempest relies and expects to continue to rely, on third parties for the manufacture of its product candidates for preclinical and clinical testing, as well as for commercial manufacture if any of its product candidates obtain marketing approval. Tempest also relies, and expects to continue to rely, on third parties to package, label, store and distribute its investigational product candidates, as well as for its commercial products if marketing approval is obtained. Tempest has internal personnel and utilizes consultants with extensive technical, manufacturing, analytical and quality experience to oversee contract manufacturing and testing activities. Tempest will continue to expand and strengthen its network of third-party providers but may also consider investing in internal manufacturing capabilities in the future if there is a technical need, or a strategic or financial benefit.

Manufacturing is subject to extensive regulations that impose procedural and documentation requirements. At a minimum these regulations govern record keeping, manufacturing processes and controls, personnel, quality control and quality assurance. Tempest’s systems, procedures and contractors are required to be in compliance with these regulations and are assessed through regular monitoring and formal audits.

Competition

The biopharmaceutical and immune-oncology industries are characterized by intense competition and rapid innovation. Any product candidates that Tempest successfully develops and commercializes will have to compete with existing and future new therapies. While Tempest believes that its technology, development experience and scientific knowledge provide it with competitive advantages, Tempest faces potential competition from many different sources, including large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

If TPST-1495, TPST-1120, or its other product candidates are approved for the treatment of tumors, they may compete with other products used to treat such diseases. There are a variety of treatments used for cancerous tumors that include chemotherapy drugs, small molecules, monoclonal antibodies, antibody-drug conjugates, bi-specific antibodies, cell therapies, oncolytic viruses and vaccines, as well as other approaches. In addition, there are several competitors in clinical development for the treatment of HCC, RCC, cholangiocarcinoma, CRC and other indications that Tempest may be targeting with TPST-1495 and TPST-1120, including companies such as Agios, Ikena, Ono, Adlai Nortye, Merck, Roche, Exelixis, and AstraZeneca.

For TPST-1495, Tempest's small molecule designed to be a dual antagonist of the EP2 and EP4 receptor, Tempest is aware of other clinical-stage EP-4-only antagonists being developed by Adlai Nortye, Ikena, and Ono. TPST-1120, Tempest's small molecule designed to be a selective antagonist of PPARα, is the first PPARα antagonist in the clinic. Tempest is not aware of other companies developing such an antagonist.

Many of Tempest's competitors, either alone or with strategic partners, have substantially greater financial, technical and human resources than Tempest does. Accordingly, Tempest's competitors may be more successful than it in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining approval for treatments and achieving widespread market acceptance, rendering Tempest's treatments obsolete or non-competitive. Merger and acquisition activity in the biotechnology and biopharmaceutical industries may result in even more resources being concentrated among a smaller number of Tempest's competitors. These companies also compete with Tempest in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials and acquiring technologies complementary to, or necessary for, Tempest's programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Tempest's commercial opportunity could be substantially limited if Tempest's competitors develop and commercialize products that are more effective, safer, less toxic, more convenient or less expensive than Tempest's comparable products. In geographies that are critical to Tempest's commercial success, competitors may also obtain regulatory approvals before it, resulting in Tempest's competitors building a strong market position in advance of the entry of its products. The key competitive factors affecting the success of all of Tempest's programs are likely to be their efficacy, safety, convenience and availability of reimbursement. In addition, Tempest's ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic drugs.

Intellectual Property

Tempest strives to protect and enhance the proprietary technology, inventions and improvements that are commercially important to its business, including obtaining, maintaining and defending its patent rights. Tempest's policy is to seek to protect its proprietary position by, among other methods, filing patent applications and obtaining issued patents in the United States and in markets outside of the United States directed to its proprietary technology, inventions, improvements and product candidates that are important to the development and implementation of its business. Tempest also relies on trade secrets and know-how relating to its proprietary technology and product candidates and continuing innovation to develop, strengthen and maintain its proprietary position in the field of oncology. Tempest also plans to rely on data exclusivity, market exclusivity and patent term extensions when available. Tempest's commercial success will depend in part on its ability to obtain and maintain patent and other proprietary protection for its technology, inventions, improvements, and product candidates; to preserve the confidentiality of its trade secrets; to defend and enforce its proprietary rights, including any patents that Tempest may own or license in the future; and to operate without infringing on the valid and enforceable patents and other proprietary rights of third parties.

As of July 9, 2021, Tempest's patent portfolio consisted of issued patents and pending patent applications that Tempest owns related to TPST-1120, TPST-1495 and various other compounds and programs. In total, as of that date, Tempest owned three issued United States patents, five pending United States patent applications, one pending international patent application filed under the Patent Cooperation Treaty (PCT application), and 24 issued patents and 29 pending patent applications in various markets outside of the United States, including Europe, China and Japan.

With respect to TPST-1120, Tempest owns issued patents and pending patent applications in the United States, Europe, China, Japan and other markets outside of the United States. The issued United States patents covering TPST-1120 as composition of matter, pharmaceutical compositions, and related methods of use are expected to expire in December 2033, absent any patent term extensions for regulatory delay. Any patents that may issue from its pending patent applications are expected to expire in December 2033, absent any patent term adjustments or patent term extensions for regulatory delay.

With respect to TPST-1495, Tempest owns an issued United States patent and pending patent applications in the United States, Europe, China, Japan and other markets outside of the United States. The issued United States patent covering TPST-1495 as composition of matter and pharmaceutical compositions is expected to expire in April 2039, absent any patent term extensions for regulatory delay.. Any patents that may issue from its pending patent applications are expected to expire between April 2038 and April 2039, absent any patent term adjustments or patent term extensions for regulatory delay.

Tempest also possesses substantial know-how and trade secrets relating to the development and commercialization of its product candidates, including related manufacturing processes and technology.

With respect to Tempest's product candidates and processes that Tempest intends to develop and commercialize in the normal course of business, Tempest intends to pursue patent protection covering, when possible, compositions, methods of use, dosing and formulations. Tempest may also pursue patent protection with respect to manufacturing and drug development processes and technologies.

Issued patents can provide protection for varying periods of time, depending upon the date of filing of the patent application, the date of patent issuance and the legal term of patents in the countries in which they are obtained. In general, patents issued for patent applications filed in the United States can provide exclusionary rights for 20 years from the earliest effective filing date. The term of United States patents may be extended by delays encountered during prosecution that are caused by the USPTO, also known as patent term adjustment. In addition, in certain instances, the term of an issued United States patent that covers or claims an FDA approved product can be extended to recapture a portion of the term effectively lost as a result of the FDA regulatory review period, which is called patent term extension. The restoration period cannot be longer than five years and the total patent term, including the restoration period, must not exceed 14 years following FDA approval. The term of patents outside of the United States varies in accordance with the laws of the foreign jurisdiction, but typically is also 20 years from the earliest effective filing date. However, the actual protection afforded by a patent varies on a product-by-product basis, from country-to-country and depends upon many factors, including the type of patent, the scope of its coverage, the availability of regulatory-related extensions, the availability of legal remedies in a particular country and the validity and enforceability of the patent.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. No consistent policy regarding the scope of claims allowable in patents in the field of oncology has emerged in the United States. The relevant patent laws and their interpretation outside of the United States are also uncertain. Changes in either the patent laws or their interpretation in the United States and other countries may diminish Tempest's ability to protect its technology or product candidates and could affect the value of such intellectual property. In particular, Tempest's ability to stop third parties from making, using, selling, offering to sell or importing products that infringe Tempest's intellectual property will depend in part on Tempest's success in obtaining and enforcing patent claims that cover its technology, inventions and improvements. Tempest cannot guarantee that patents will be granted with respect to any of its pending patent applications or with respect to any patent applications Tempest may file in the future, nor can Tempest be sure that any patents that may be granted to Tempest in the future will be commercially useful in protecting its products, the methods of use or manufacture of those products.

Moreover, even its issued patents may not guarantee Tempest the right to practice its technology in relation to the commercialization of its products. Patent and other intellectual property rights in the pharmaceutical and biotechnology space are evolving and involve many risks and uncertainties. For example, third parties may have blocking patents that could be used to prevent Tempest from commercializing its product candidates and practicing its proprietary technology, and its issued patents may be challenged, invalidated or circumvented, which could limit Tempest's ability to stop competitors from marketing related products or could limit the term of patent protection that otherwise may exist for its product candidates. In addition, the scope of the rights granted under any issued patents may not provide Tempest with protection or competitive advantages against competitors with similar technology. Furthermore, Tempest's competitors may independently develop similar technologies that are outside the scope of the rights granted under any issued patents. For these reasons, Tempest may face competition with respect to its product candidates. Moreover, because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that, before any particular product candidate can be commercialized, any patent protection for such product may expire or remain in force for only a short period following commercialization, thereby reducing the commercial advantage the patent provides.

Government regulation

Government authorities in the United States at the federal, state and local level and in other countries and jurisdictions extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, post-approval monitoring and reporting, marketing and export and import of pharmaceutical products, such as Tempest's investigational medicines and any future investigational medicines. Generally, before a new pharmaceutical product can be marketed, considerable data demonstrating its quality, safety and efficacy must be obtained, organized into a format specific for each regulatory authority, submitted for review and approved by the regulatory authority.

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the Food and Drug Administration, or FDA, the Federal Food, Drug, and Cosmetic Act, or FD&C Act, and other federal and state statutes and regulations govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as clinical hold, FDA refusal to approve pending New Drug Applications, or NDAs, warning or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties and criminal prosecution.

Tempest's investigational medicines and any future investigational medicines must be approved by the FDA pursuant to a NDA before they may be legally marketed in the United States. The process generally involves the following:

- Completion of extensive preclinical laboratory and animal studies in accordance with applicable regulations, including studies conducted in accordance with Good Laboratory Practice, or GLP, requirements
- Submission to the FDA of an Investigational New Drug application, or IND, which must become effective before human clinical trials may begin;
- Approval by an Institutional Review Board (IRB) or independent ethics committee at each clinical trial site before each clinical trial may be commenced;
- Performance of adequate and well-controlled human clinical trials in accordance with applicable IND regulations, Good Clinical Practice (GCP) requirements and other clinical trial-related regulations to establish the safety and efficacy of the investigational product for each proposed indication;
- Submission to the FDA of an NDA;
- Payment of any user fees for FDA review of the NDA;
- A determination by the FDA within 60 days of its receipt of a NDA to accept the filing for review;
- Satisfactory completion of one or more FDA pre-approval inspections of the manufacturing facility or facilities where the drug, or components thereof, will be produced to assess compliance with cGMP requirements to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity;
- Satisfactory completion of any potential FDA audits of the clinical trial sites that generated the data in support of the NDA to assure compliance with GCPs and integrity of the clinical data;
- FDA review and approval of the NDA, including consideration of the views of any FDA advisory committee; and
- Compliance with any post-approval requirements, including REMS, where applicable, and post- approval studies required by the FDA as a condition of approval.

The preclinical and clinical testing and approval process requires substantial time, effort and financial resources, and Tempest cannot be certain that any approvals for its product candidates will be granted on a timely basis, or at all.

Preclinical Studies

Before testing any drug product candidates in humans, the product candidate must undergo rigorous preclinical testing. Preclinical tests include laboratory evaluation of product chemistry, formulation and toxicity, as well as in vitro and animal studies to assess the potential for adverse events and in some cases to establish a rationale for therapeutic use. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical studies, among other things, to the FDA as part of an IND. An IND is a request for authorization from the FDA to administer an investigational product to humans and must become effective before human clinical trials may begin. Some long-term preclinical testing may continue after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the trial on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator, generally a physician not employed by or under the trial sponsor's control. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with GCPs, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators and monitors; as well as (iii) under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated in the trial. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND. Furthermore, each clinical trial must be reviewed and approved by an IRB for each institution at which the clinical trial will be conducted to ensure that the risks to individuals participating in the clinical trials are minimized and are reasonable in relation to anticipated benefits. The IRB also approves the informed consent form that must be provided to each clinical trial subject or his or her legal representative and must monitor the clinical trial until completed.

There also are requirements governing the reporting of ongoing clinical trials and completed clinical trial results to public registries. Information about certain clinical trials, including clinical trial results, must be submitted within specific timeframes for publication on the www.clinicaltrials.gov website. Information related to the product, patient population, phase of investigation, clinical trial sites and investigators and other aspects of the clinical trial is then made public as part of the registration. Disclosure of the results of these clinical trials can be delayed in certain circumstances for up to two years after the date of completion of the trial.

A sponsor who wishes to conduct a clinical trial outside of the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of an NDA. The FDA will accept a well- designed and well-conducted foreign clinical trial not conducted under an IND if the clinical trial was conducted in accordance with GCP requirements, and the FDA is able to validate the data through an onsite inspection if deemed necessary.

Clinical trials are generally conducted in three sequential phases, known as Phase 1, Phase 2 and Phase 3:

- Phase 1 clinical trials generally involve a small number of healthy volunteers or disease-affected patients who are initially exposed to a single dose and then multiple doses of the product candidate. The primary purpose of these clinical trials is to assess the metabolism, pharmacokinetics, pharmacologic action, side effect tolerability, safety of the product candidate, and, if possible, early evidence of effectiveness.
- Phase 2 clinical trials generally involve studies in disease-affected patients to evaluate proof of concept and/or determine the dosing regimen(s) for subsequent investigations. At the same time, safety and further pharmacokinetic and pharmacodynamic information is collected, possible adverse effects and safety risks are identified, and a preliminary evaluation of efficacy is conducted.

- Phase 3 clinical trials generally involve a large number of patients at multiple sites and are designed to provide the data necessary to demonstrate the effectiveness of the product for its intended use, its safety in use and to establish the overall benefit/risk relationship of the product and provide an adequate basis for product labeling. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug.

These Phases may overlap or be combined. For example, a Phase 1/2 clinical trial may contain both a dose-escalation stage and a dose expansion stage, the latter of which may confirm tolerability at the recommended dose for expansion in future clinical trials (as in traditional Phase 1 clinical trials) and provide insight into the anti-tumor effects of the investigational therapy in selected subpopulation(s).

Typically, during the development of oncology therapies, all subjects enrolled in Phase 1 clinical trials are disease-affected patients and, as a result, considerably more information on clinical activity may be collected during such trials than during Phase 1 clinical trials for non-oncology therapies. A single Phase 3 or Phase 2 trial with other confirmatory evidence may be sufficient in rare instances to provide substantial evidence of effectiveness (generally subject to the requirement of additional post-approval studies). The manufacturer of an investigational drug in a phase 2 or 3 clinical trial for a serious or life-threatening disease is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for expanded access.

Phase 1, Phase 2, Phase 3 and other types of clinical trials may not be completed successfully within any specified period, if at all. The FDA, the IRB, or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including non-compliance with regulatory requirements or a finding that the patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether a trial may move forward at designated checkpoints based on access to certain data from the trial.

Concurrent with clinical trials, companies usually complete additional animal studies and also must develop additional information about the chemistry and physical characteristics of the drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product and, among other things, companies must develop methods for testing the identity, strength, quality, potency and purity of the final product. Additionally, appropriate packaging must be selected and tested, and stability studies must be conducted to demonstrate that the investigational medicines do not undergo unacceptable deterioration over their shelf life.

FDA Review Process

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture and controls. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and efficacy of the investigational product to the satisfaction of the FDA. FDA approval of a NDA must be obtained before a drug may be marketed in the United States. The cost of preparing and submitting an NDA is substantial. Under the PDUFA, each NDA must be accompanied by a substantial user fee. The FDA adjusts the PDUFA user fees on an annual basis. Fee waivers or reductions are available in certain circumstances, including a waiver of the application fee for the first application filed by a small business. Additionally, no user fees are assessed on NDAs for products designated as orphan drugs, unless the product also includes a non-orphan indication. The applicant under an approved NDA is also subject to an annual program fee.

The FDA reviews each submitted NDA before it determines whether to file it and may request additional information. The FDA must make a decision on whether to file an NDA within 60 days of receipt, and such decision could include a refusal to file by the FDA. Once the submission is filed, the FDA begins an in-depth review of the NDA. The FDA has agreed to certain performance goals in the review of NDAs. Most applications for standard review drug products are reviewed within ten to twelve months; most applications for priority review drugs are reviewed in six to eight months. Priority review can be applied to drugs that the FDA determines may offer significant improvement in safety or effectiveness compared to marketed products or where no adequate therapy exists. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission. The FDA does not always meet its goal dates for standard and priority NDAs, and the review process can be extended by FDA requests for additional information or clarification.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an outside advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation and a recommendation as to whether the application should be approved and under what conditions, if any. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations.

Before approving an NDA, the FDA will conduct a pre-approval inspection of the manufacturing facilities for the new product to determine whether they comply with cGMP requirements. The FDA will not approve the product unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. The FDA also typically inspects clinical trial sites to ensure compliance with GCP requirements and the integrity of the data supporting safety and efficacy.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter, or CRL, generally outlines the deficiencies in the submission and may require substantial additional testing, or information, in order for the FDA to reconsider the application, such as additional clinical data, additional pivotal clinical trial(s), and/or other significant and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. If a CRL is issued, the applicant may resubmit the NDA addressing all of the deficiencies identified in the letter, withdraw the application, engage in formal dispute resolution or request an opportunity for a hearing. The FDA has committed to reviewing resubmissions in two or six months depending on the type of information included. Even if such data and information are submitted, the FDA may decide that the NDA does not satisfy the criteria for approval.

As a potential condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks to patients. A REMS can include medication guides, communication plans for healthcare professionals and elements to assure a product's safe use (ETASU). An ETASU can include, but is not limited to, special training or certification for prescribing or dispensing the product, dispensing the product only under certain circumstances, special monitoring and the use of patient-specific registries. The requirement for a REMS can materially affect the potential market and profitability of the product. Moreover, the FDA may require substantial post-approval testing and surveillance to monitor the product's safety or efficacy.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of an NDA supplement or, in some case, a new NDA, before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition, which is generally a disease or condition that affects fewer than 200,000 individuals in the United States, or more than 200,000 individuals in the United States but for which there is no reasonable expectation that the cost of developing and making the product for this type of disease or condition will be recovered from sales of the product in the United States.

Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the drug and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

If a product that has orphan designation subsequently receives the first FDA approval for the disease or condition for which it has such designation, the product is entitled to a seven-year exclusive marketing period in the U.S. for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity by means of greater effectiveness, greater safety, or providing a major contribution to patient care, or in instances of drug supply issues. Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition, or the same drug for a different disease or condition. Other benefits of orphan drug designation include tax credits for certain research and an exemption from the NDA user fee.

Expedited Development and Review Programs

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition.

Fast Track Designation

Fast track designation may be granted for products that are intended to treat a serious or life-threatening disease or condition for which there is no effective treatment and preclinical or clinical data demonstrate the potential to address unmet medical needs for the condition. Fast track designation applies to both the product and the specific indication for which it is being studied. The sponsor of an investigational drug product may request that the FDA designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the submission of the IND for the drug candidate. The FDA must determine if the drug candidate qualifies for fast track designation within 60 days of receipt of the sponsor's request. For fast track products, sponsors may have greater interactions with the FDA and the FDA may initiate review of sections of a fast track product's NDA before the application is complete. This rolling review is available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a fast track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information and the sponsor must pay applicable user fees. At the time of NDA filing, the FDA will determine whether to grant priority review designation. Additionally, fast track designation may be withdrawn if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Breakthrough Therapy Designation

Breakthrough therapy designation may be granted for products that are intended, alone or in combination with one or more other products, to treat a serious or life-threatening condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over currently approved therapies on one or more clinically significant endpoints. Under the breakthrough therapy program, the sponsor of a new drug candidate may request that the FDA designate the candidate for a specific indication as a breakthrough therapy concurrent with, or after, the submission of the IND for the drug candidate. The FDA must determine if the drug product qualifies for breakthrough therapy designation within 60 days of receipt of the sponsor's request. The FDA may take certain actions with respect to breakthrough therapies, including holding meetings with the sponsor throughout the development process, providing timely advice to the product sponsor regarding development and approval, involving more senior staff in the review process, assigning a cross-disciplinary project lead for the review team and taking other steps to design the clinical studies in an efficient manner.

Priority Review

Priority review may be granted for products that are intended to treat a serious or life-threatening condition and, if approved, would provide a significant improvement in safety and effectiveness compared to available therapies. The FDA will attempt to direct additional resources to the evaluation of an application designated for priority review in an effort to facilitate the review.

Accelerated Approval

Accelerated approval may be granted for products that are intended to treat a serious or life-threatening condition and that generally provide a meaningful therapeutic advantage to patients over existing treatments. A product eligible for accelerated approval may be approved on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions or survives. The accelerated approval pathway is most often used in settings in which the course of a disease is long, and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large studies to demonstrate a clinical or survival benefit. The accelerated approval pathway is contingent on a sponsor's agreement to conduct additional post-approval confirmatory studies to verify and describe the product's clinical benefit. These confirmatory trials must be completed with due diligence and, in some cases, the FDA may require that the trial be designed, initiated and/or fully enrolled prior to approval. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, would allow the FDA to withdraw the product from the market on an expedited basis. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

Even if a product qualifies for one or more of these programs, the FDA may later decide that the product no longer meets the conditions for qualification or the time period for FDA review or approval may not be shortened. Furthermore, fast track designation, breakthrough therapy designation, priority review and accelerated approval do not change the standards for approval, but may expedite the development or approval process.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted, with certain exceptions.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity—patent or nonpatent—for a drug if certain conditions are met. Conditions for exclusivity include the FDA's determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Post-Approval Requirements

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs may be marketed only for the approved indications and in a manner consistent with the approved labeling.

Adverse event reporting and submission of periodic reports are required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as phase 4 testing, risk evaluation and mitigation strategies, or REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging and labeling procedures must continue to conform to cGMPs after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the Agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information, imposition of post-market studies or clinical studies to assess new safety risks or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- Restrictions on the marketing or manufacturing of the product, suspension of the approval, complete withdrawal of the product from the market or product recalls;
- Fines, warning or other enforcement-related letters or holds on post-approval clinical studies;
- Refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product license approvals;
- Product seizure or detention, or refusal to permit the import or export of products; or
- Injunctions or the imposition of civil or criminal penalties.

The Hatch-Waxman Act

Orange Book Listing

Under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch Waxman Amendments, NDA applicants are required to identify to the FDA each patent whose claims cover the applicant's drug or approved method of using the drug. Upon approval of a drug, the applicant must update its listing of patents to the NDA in timely fashion and each of the patents listed in the application for the drug is then published in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book.

Drugs listed in the Orange Book can, in turn, be cited by potential generic competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredient(s), strength, route of administration, and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. An approved ANDA product is considered to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved under the ANDA pathway are commonly referred to as "generic equivalents" to the listed drug and can often be substituted by pharmacists under prescriptions written for the original listed drug pursuant to each state's laws on drug substitution.

The ANDA applicant is required to certify to the FDA concerning any patents identified for the reference listed drug in the Orange Book. Specifically, the applicant must certify to each patent in one of the following ways: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. For patents listed that claim an approved method of use, under certain circumstances the ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than certify to a listed method-of-use patent. If the applicant does not challenge the listed patents through a Paragraph IV certification, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA-holder and patentee(s) once the ANDA has been accepted for filing by the FDA (referred to as the "notice letter"). The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice letter. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months from the date the notice letter is received, expiration of the patent, the date of a settlement order or consent decree signed and entered by the court stating that the patent that is the subject of the certification is invalid or not infringed, or a decision in the patent case that is favorable to the ANDA applicant.

The ANDA application also will not be approved until any applicable non-patent exclusivity listed in the Orange Book for the referenced product has expired. In some instances, an ANDA applicant may receive approval prior to expiration of certain non-patent exclusivity if the applicant seeks, and the FDA permits, the omission of such exclusivity-protected information from the ANDA prescribing information.

Exclusivity

Upon NDA approval of a new chemical entity, or NCE, which is a drug that contains no active moiety that has been approved by the FDA in any other NDA, that drug receives five years of marketing exclusivity during which the FDA cannot receive any ANDA seeking approval of a generic version of that drug unless the application contains a Paragraph IV certification, in which case the application may be submitted one year prior to expiration of the NCE exclusivity. If there is no listed patent in the Orange Book, there may not be a Paragraph IV certification, and, thus, no ANDA for a generic version of the drug may be filed before the expiration of the exclusivity period.

Certain changes to an approved drug, such as the approval of a new indication, the approval of a new strength, and the approval of a new condition of use, are associated with a three-year period of exclusivity from the date of approval during which the FDA cannot approve an ANDA for a generic drug that includes the change. In some instances, an ANDA applicant may receive approval prior to expiration of the three-year exclusivity if the applicant seeks, and the FDA permits, the omission of such exclusivity-protected information from the ANDA package insert.

Patent Term Extension

The Hatch Waxman Amendments permit a patent term extension as compensation for patent term lost during the FDA regulatory review process. Patent term extension, however, cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. After NDA approval, owners of relevant drug patents may apply for the extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval) up to a maximum of five years. The time can be reduced for any time the FDA determines that the applicant did not pursue approval with due diligence.

The United States Patent and Trademark Office, or USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. However, the USPTO may not grant an extension because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than requested.

The total patent term after the extension may not exceed 14 years, and only one patent can be extended. The application for the extension must be submitted prior to the expiration of the patent, and for patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the USPTO must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

Other Healthcare Laws

In addition to FDA restrictions on marketing of pharmaceutical products, several other state and federal laws have been applied to restrict certain general business and marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes, false claims statutes and other healthcare laws and regulations.

The federal Anti-Kickback Statute is a criminal law that prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. Although there are a number of statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions under the law, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. In addition, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to commit a violation.

Federal civil and criminal false claims laws, including the federal civil False Claims Act, prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. This includes claims made to programs where the federal government reimburses for the product, such as Medicare and Medicaid, as well as programs where the federal government is a direct purchaser, such as when it purchases off the Federal Supply Schedule. Several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. Additionally, the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act. Most states also have statutes or regulations similar to the federal Anti-Kickback Statute and civil False Claims Act, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Other federal statutes pertaining to healthcare fraud and abuse include the civil monetary penalties statute, which prohibits, among other things, the offer or payment of remuneration to a Medicaid or Medicare beneficiary that the offeror or payor knows or should know is likely to influence the beneficiary to order a receive a reimbursable item or service from a particular supplier, and the additional federal criminal statutes created by the Health Insurance Portability and Accountability Act of 1996, or HIPAA, which prohibits, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or obtain by means of false or fraudulent pretenses, representations or promises any money or property owned by or under the control of any healthcare benefit program in connection with the delivery of or payment for healthcare benefits, items or services. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to commit a violation. Further, as promulgated under the Patient Protection and Affordable Care Act (“ACA”), the federal Physician Payment Sunshine Act requires manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid or the Children’s Health Insurance Program to collect and report information on certain payments or transfers of value to physicians and teaching hospitals, as well as investment interests held by physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and their immediate family members. The first reports were due in 2014 and must be submitted on an annual basis thereafter. The reported data is made available in searchable form on a public website on an annual basis. Failure to submit required information may result in civil monetary penalties. Effective January 1, 2022, reporting on payments or transfers of value to physician assistants, nurse practitioners or clinical nurse specialists, certified registered nurse anesthetists, and certified nurse-midwives will also be required.

In addition, several states now require prescription drug companies to report certain expenses relating to the marketing and promotion of drug products and to report gifts and payments to individual healthcare practitioners in these states. Other states prohibit various marketing-related activities, such as the provision of certain kinds of gifts or meals. Still other states require the posting of information relating to clinical studies and their outcomes. Some states require the reporting of certain drug pricing information, including information pertaining to and justifying price increases. In addition, states such as California, Connecticut, Nevada and Massachusetts require pharmaceutical companies to implement compliance programs and/or marketing codes. Several additional states are considering similar proposals. Certain states and local jurisdictions also require the registration of pharmaceutical sales and medical representatives. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

Efforts to ensure that business arrangements with third parties comply with applicable healthcare laws and regulations involve substantial costs. If a drug company's operations are found to be in violation of any such requirements, it may be subject to significant penalties, including civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, the curtailment or restructuring of its operations, loss of eligibility to obtain approvals from the FDA, exclusion from participation in government contracting, healthcare reimbursement or other federal or state government healthcare programs, including Medicare and Medicaid, integrity oversight and reporting obligations, imprisonment, and reputational harm. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action for an alleged or suspected violation can cause a drug company to incur significant legal expenses and divert management's attention from the operation of the business, even if such action is successfully defended.

U.S. Healthcare Reform

In the United States there have been, and continue to be, proposals by the federal government, state governments, regulators and third-party payors to control or manage the increased costs of health care and, more generally, to reform the U.S. healthcare system. The pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. For example, in March 2010, the ACA was enacted, which intended to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for the healthcare and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms, substantially changed the way healthcare is financed by both governmental and private insurers, and significantly impacts the U.S. pharmaceutical industry. The ACA, among other things, (i) subjected therapeutic biologics to potential competition by lower-cost biosimilars by creating a licensure framework for follow-on biologic products, (ii) proscribed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs and therapeutic biologics that are inhaled, infused, instilled, implanted or injected, (iii) increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program and extended the rebate program to individuals enrolled in Medicaid managed care organizations, (iv) established annual nondeductible fees and taxes on manufacturers of certain branded prescription drugs and therapeutic biologics, apportioned among these entities according to their market share in certain government healthcare programs, (v) established a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% (now 70%) point of-sale discounts off negotiated prices of applicable brand drugs and therapeutic biologics to eligible beneficiaries during their coverage gap period, as a condition for the manufacturer's outpatient drugs and therapeutic biologics to be covered under Medicare Part D, (vi) expanded eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new mandatory eligibility categories for individuals with income at or below 133% of the federal poverty level, thereby potentially increasing manufacturers' Medicaid rebate liability, (vii) expanded the entities eligible for discounts under the Public Health program, (viii) created a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research, and (ix) established a Center for Medicare Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending, potentially including prescription drug spending.

The Trump administration and former Congress sought to modify, repeal, or otherwise invalidate all, or certain provisions of, the ACA. By way of example, the Tax Cuts and Jobs Act of 2017, or the Tax Act, was enacted and included, among other things, a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". There have been subsequent challenges to the constitutionality of the ACA following the repeal of the individual mandate. On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the Affordable Care Act brought by several states without specifically ruling on the constitutionality of the law. It is also unclear how future efforts to repeal, replace or challenge the ACA will impact the ACA. Tempest cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on its business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted to reduce healthcare expenditures. United States federal government agencies also currently face potentially significant spending reductions, which may further impact healthcare expenditures. On August 2, 2011, the Budget Control Act of 2011, among other things, included aggregate reductions of Medicare payments to providers of 2% per fiscal year. These reductions went into effect on April 1, 2013 and, due to subsequent legislative amendments to the statute will remain in effect into 2031, with the exception of a temporary suspension from May 1, 2020 through December 31, 2021, unless additional Congressional action is taken. Moreover, on January 2, 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers, including hospitals, imaging centers and cancer treatment centers, and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. If federal spending is further reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or the National Institutes of Health to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve research and development, manufacturing, and marketing activities, which may delay Tempest's ability to develop, market and sell any products Tempest may develop.

Moreover, payment methodologies may be subject to changes in healthcare legislation and regulatory initiatives. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for physician-administered drugs. In addition, this legislation provided authority for limiting the number of drugs that will be covered in any therapeutic class. While the MMA only applies to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates. Therefore, any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payors.

Recently there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products, which has resulted in several Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drug products. The Biden administration has begun taking executive actions to address drug pricing and other healthcare policy changes, though it remains unclear whether the Biden administration will work to reverse the measures taken by the Trump administration or pursue similar policy initiatives. On July 9, 2021, President Biden signed an executive order to promote competition in the U.S. economy that included several initiatives aimed prescription drugs. Among other provisions, the executive order directed the Secretary of HHS to issue a report to the White House within 45 days that includes a plan to, among other things, reduce prices for prescription drugs, including prices paid by the federal government for such drugs. At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn, and Matthew Bellina Right to Try Act of 2017 was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA authorization under an FDA expanded access program; however, manufacturers are not obligated to provide investigational new drug products under the current federal right to try law.

Facilities

Tempest's corporate headquarters are located at 7000 Shoreline Court, Suite 275, South San Francisco, California 94080 where it occupies approximately 9,780 square feet of research and development laboratory and related office space under a lease that ends in February 2024. Tempest believes that its existing facilities meet its current needs. Tempest may need additional office space in the future as it continues to build its development, commercial and support teams. Tempest believes that it can find suitable additional space in the future on commercially reasonable terms.

Employees

As of July 9, 2021, Tempest had 15 employees, including nine holding Ph.D., M.D., JD, LL.M., and/or MBA degrees. Tempest's employees have established expertise in chemistry, biochemistry, molecular biology, immunology, pharmacology, toxicology, pre-clinical development, regulatory and quality, translational medicine, and early-to-late-stage clinical development, as well as finance, business development and strategic transactions. None of Tempest's employees are represented by a labor union or covered by collective bargaining agreements. Tempest will continue to add experienced and talented scientists in areas, such as medicinal chemistry, that Tempest believes are critical for the discovery of highly differentiated small-molecule compounds.

Legal Proceedings

For information on our existing legal proceedings, see the information set forth under the heading "Litigation" in Note 6, Commitments and Contingencies, in Notes to Unaudited Interim Consolidated Financial Statements in Item 1 of Part I of our Quarterly Report on Form 10-Q, filed on May 13, 2021.

Furthermore, since May 13, 2021, the following updates have occurred in relation to the Dahhan Action: on May 28, 2021, the court denied the motion to strike the second amended complaint and motions to dismiss by the other defendants; on June 7, 2021, the court lifted the stay and established a revised case schedule; on June 29, 2021, after the parties agreed that the seal was no longer necessary, the lead plaintiff publicly filed its second amended complaint; and defendants filed their answers and affirmative defenses to the second amended complaint on July 13, 2021.

In addition, from time to time, we are involved in litigation or other legal proceedings as part of our ordinary course of business.

RISK FACTORS

You should carefully consider the risks described below. The occurrence of any of the following risks could have a material adverse effect on our business, financial condition, results of operations and future growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made or may make from time to time. In these circumstances, the market price of our common stock could decline, and you may lose all or part of your investment. We cannot assure you that any of the events discussed below will not occur. Such risks may be amplified by the COVID-19 pandemic and its potential impact on our business and the global economy.

Unless otherwise stated in these risk factors or the context otherwise requires, references in these risk factors to:

- "Tempest" refers to Tempest Therapeutics, Inc., a Delaware corporation, known before June 25, 2021 as Millendo Therapeutics, Inc.
- "Millendo" refers to Millendo Therapeutics, Inc., a Delaware corporation, prior to the Merger. On June 25, 2021, Millendo effected a 1-for-15 reverse stock split of its common stock, completed the Merger and changed its name to "Tempest Therapeutics, Inc."
- "Private Tempest" refers to TempestTx, Inc., previously known as "Tempest Therapeutics, Inc."
- "Merger" refers to the series of transaction, completed on June 25, 2021, on which, among other things, Mars Merger Corp., a Delaware corporation and subsidiary of Millendo, merged with and into Private Tempest, with Private Tempest continuing as the wholly owned subsidiary of Millendo and the surviving corporation of the merger. Following the completion of the Merger, the business conducted by Tempest became the business conducted by Private Tempest.
- References to "we," "our," "us" and the "company" in this document refer to Tempest.

Summary Risk Factors

- Tempest has a history of operating losses, and Tempest may not achieve or sustain profitability. Tempest anticipates that it will continue to incur losses for the foreseeable future. If Tempest fails to obtain additional funding to conduct its planned research and development efforts, Tempest could be forced to delay, reduce or eliminate Tempest's product development programs or commercial development efforts.
- Tempest expects that it will need to raise additional funding before Tempest can expect to become profitable from any potential future sales of Tempest's product candidates. This additional financing may not be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force Tempest to delay, limit or terminate its product development efforts or other operations.
- If Tempest is unable to develop, obtain regulatory approval for and commercialize TPST-1495 and TPST-1120 and its future product candidates, or if Tempest experiences significant delays in doing so, Tempest's business will be materially harmed.
- Success in preclinical studies and earlier clinical trials for Tempest's product candidates may not be indicative of the results that may be obtained in later clinical trials, which may delay or prevent obtaining regulatory approval.

- The commercial success of Tempest's product candidates, including TPST-1495 and TPST-1120, will depend upon their degree of market acceptance by providers, patients, patient advocacy groups, third-party payors and the general medical community.
- Tempest faces significant competition in an environment of rapid technological change, and it is possible that Tempest's competitors may achieve regulatory approval before Tempest or develop therapies that are more advanced or effective than Tempest's, which may harm Tempest's business, financial condition and Tempest's ability to successfully market or commercialize TPST-1495, TPST-1120, and Tempest's other product candidates.
- If Tempest is unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell Tempest's product candidates, Tempest may be unable to generate any revenues.
- The FDA regulatory approval process is lengthy and time-consuming, and Tempest may experience significant delays in the clinical development and regulatory approval of Tempest's product candidates.
- Tempest expects to expand its development and regulatory capabilities, and as a result, Tempest may encounter difficulties in managing its growth, which could disrupt Tempest's operations.
- Private Tempest and Millendo may be unable to integrate successfully and realize the anticipated benefits of the Merger.

We have a history of operating losses, and we may not achieve or sustain profitability. We anticipate that we will continue to incur losses for the foreseeable future. If we fail to obtain additional funding to conduct our planned research and development efforts, we could be forced to delay, reduce or eliminate our product development programs or commercial development efforts.

We are a clinical-stage biotechnology company with a limited operating history. Biotechnology product development is a highly speculative undertaking and involves a substantial degree of risk. Our operations to date have been limited primarily to organizing and staffing, business planning, raising capital, acquiring and developing product and technology rights, manufacturing, and conducting research and development activities for our product candidates. We have never generated any revenue from product sales and we have not obtained regulatory approvals for any of our product candidates. Private Tempest has incurred net losses in each year since its inception.

Private Tempest incurred net losses of $14.4 million and $19.2 million for the year ended December 31, 2019 and the year ended December 31, 2020, respectively. As of December 31, 2020, Private Tempest had an accumulated deficit of $71.8 million. Substantially all of Private Tempest's operating losses have resulted from costs incurred in connection with Private Tempest's research and development programs and from general and administrative costs associated with Private Tempest's operations. We expect to continue to incur significant expenses and operating losses over the next several years and for the foreseeable future as we intend to continue to conduct research and development, clinical testing, regulatory compliance activities, manufacturing activities, and, if any of our product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in Tempest incurring significant losses for the foreseeable future. Privat Tempest's prior losses, combined with our expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital.

Millendo's net loss was $36.4 million and $44.6 million and for the years ended December 31, 2020 and 2019, respectively. As of December 31, 2020, Millendo had an accumulated deficit of $245.1 million.

We expect that it will need to raise additional funding before we can expect to become profitable from any potential future sales of our product candidates. This additional financing may not be available on acceptable terms or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We will require substantial future capital in order to complete planned and future preclinical and clinical development for our product candidates and potentially commercialize these product candidates. Based upon our current operating plan, we believe that our cash and cash equivalents as of March 31, 2021 of $27.4 million, will enable us to fund our operating expenses and capital expenditure requirements through into early 2023. We expect our spending levels to increase in connection with our preclinical studies and clinical trials of our product candidates. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant expenses related to commercial launch, product sales, medical affairs, marketing, manufacturing and distribution. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with its continuing operations before any commercial revenue may occur.
Additional capital might not be available when we need it and our actual cash requirements might be greater than anticipated. If we require additional capital at a time when investment in its industry or in the marketplace in general is limited, we might not be able to raise funding on favorable terms, if at all. If we are not able to obtain financing when needed or on terms favorable to us, we may need to delay, reduce or eliminate certain research and development programs or other operations, sell some or all of our assets or merge with another entity.

Tempest's operations have consumed significant amounts of cash since inception. Tempest's future capital requirements will depend on many factors, including:

- the costs associated with the scope, progress and results of discovery, preclinical development, laboratory testing and clinical trials for Tempest's product candidates;
- the costs associated with the manufacturing of Tempest's product candidates;
- the costs related to the extent to which Tempest enters into partnerships or other arrangements with third parties to further develop Tempest's product candidates;
- the costs and fees associated with the discovery, acquisition or in-license of product candidates or technologies;
- Tempest's ability to establish collaborations on favorable terms, if at all;
- the costs of future commercialization activities, if any, including product sales, marketing, manufacturing and distribution, for any of Tempest's product candidates for which Tempest receives marketing approval;
- revenue, if any, received from commercial sales of Tempest's product candidates, should any of Tempest's product candidates receive marketing approval; and
- the costs of preparing, filing and prosecuting patent applications, maintaining and enforcing Tempest's intellectual property rights and defending intellectual property-related claims.

Tempest's product candidates, if approved, may not achieve commercial success. Tempest's commercial revenues, if any, will be derived from sales of product candidates that Tempest does not expect to be commercially available for many years, if at all. Accordingly, Tempest will need to continue to rely on additional financing to achieve Tempest's business objectives, which may not be available to Tempest on acceptable terms, or at all.

If we fail to maintain proper and effective internal controls, our ability to produce accurate financial statements on a timely basis could be impaired.

We are subject to the reporting requirements of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, and the rules and regulations of the stock market on which our common stock is listed. The Sarbanes-Oxley Act requires, among other things, that we maintain effective disclosure controls and procedures and internal control over financial reporting and that, after a transitional period, we furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment includes disclosure of any material weaknesses identified by our management in our internal control over financial reporting. However, due to recent changes in SEC rules related to smaller reporting companies, Millendo was not required to have its auditors formally attest to the effectiveness of its internal control over financial reporting in connection with this Annual Report on Form 10-K for the year ended December 31, 2020. Additionally, we will not be required to have our auditors formally attest to the effectiveness of our internal control over financial reporting until we cease to be a smaller reporting company.

We may identify weaknesses in our system of internal financial and accounting controls and procedures that could result in a material misstatement of our financial statements. Our internal control over financial reporting will not prevent or detect all errors and all fraud. A control system, no matter how well designed and operated, can provide only reasonable, not absolute, assurance that the control system's objectives will be met. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that misstatements due to error or fraud will not occur or that all control issues and instances of fraud will be detected.

If we are not able to comply with the requirements of Section 404 of the Sarbanes-Oxley Act, or Section 404, in a timely manner, or if we are unable to maintain proper and effective internal controls, we may not be able to produce timely and accurate financial statements. If that were to happen, the market price of our stock could decline and we could be subject to sanctions or investigations by the stock exchange on which our common stock is listed, the Securities and Exchange Commission ("SEC"), or other regulatory authorities.

Additionally, as a privately held company, Private Tempest was not required to evaluate its internal control over financial reporting in a manner that meets the standards of publicly traded companies required by Section 404. In preparing Private Tempest's financial statements as of and for the year ended December 31, 2020, management of Private Tempest identified material weaknesses in its internal control over financial reporting. We cannot assure you that the material weaknesses identified at Private Tempest will be remediated by Tempest on the timelines currently anticipated, or at all, and/or that there will not be additional material weaknesses or significant deficiencies in the internal control over financial reporting in the future. Any failure to maintain effective internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if the company's independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins its reporting on internal control over financial reporting, investors may lose confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

Private Tempest had identified material weaknesses in its internal control over financial reporting. Failure to achieve and maintain effective internal control over financial reporting could harm our business and negatively impact the value of our common stock.

Private Tempest had identified material weaknesses in its internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting, such that there is a reasonable possibility that a material misstatement of Private Tempest's annual or interim financial statements will not be prevented or detected on a timely basis. In preparing Private Tempest's financial statements as of and for the year ended December 31, 2020, management of Private Tempest identified the following material weaknesses in its internal control over financial reporting:

- Private Tempest did not have sufficient resources with appropriate knowledge and expertise to design, implement, document and operate effective internal controls over financial reporting.
- Private Tempest did not design and implement controls surrounding review of clinical trial expenses, including the evaluation of the terms of its clinical trial contracts. Specifically, Private Tempest failed to properly review and evaluate the progress of expenses incurred in its clinical trial contracts that resulted in the inaccurate accrual of clinical trial expenses.

These material weaknesses resulted in adjustments to Private Tempest's financial statements. Additionally, these material weaknesses could result in a misstatement of Private Tempest's accounts or disclosures that would result in a material misstatement of its annual or interim financial statements that would not be prevented or detected, and accordingly, Private Tempest determined that these control deficiencies constitute material weaknesses.

Tempest is actively recruiting additional accounting personnel with appropriate experience, certification, education and training as a component of its plans to remediate the material weaknesses. Tempest also plans to design and implement controls related to review of clinical trial expenses to properly evaluate progress of expense incurred in clinical trial contracts. To the extent that Tempest is not able to hire and retain such individuals, or is unable to successfully design and implement such controls, the material weaknesses identified may not be remediated and management may be required to record additional adjustments to its financial statements in the future.

Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.

Tempest's operations to date have been limited to organizing and staffing Tempest, business planning, raising capital, acquiring Tempest's technology, identifying potential product candidates, undertaking research and preclinical studies of Tempest's product candidates, manufacturing, and establishing licensing arrangements. Tempest has not yet demonstrated the ability to complete clinical trials of Tempest's product candidates, obtain marketing approvals, manufacture a commercial scale product or conduct sales and marketing activities necessary for successful commercialization. Consequently, any predictions you make about Tempest's future success or viability may not be as accurate as they could be if Tempest had a longer operating history.

In addition, as a new business, Tempest may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. Tempest will need to transition from a company with a licensing and research focus to a company that is also capable of supporting clinical development and commercial activities. Tempest may not be successful in such a transition.

Risks Related to Tempest's Product Development and Regulatory Approval

If Tempest is unable to develop, obtain regulatory approval for and commercialize TPST-1495 and TPST-1120 and its future product candidates, or if Tempest experiences significant delays in doing so, Tempest's business will be materially harmed.

Tempest plans to invest a substantial amount of its efforts and financial resources in its current lead product candidates, TPST-1495, a dual EP2/EP4 prostaglandin (PGE2) receptor antagonist, and TPST-1120, a peroxisome proliferator-activated receptor alpha (PPARα) antagonism for the treatment of various cancers. Tempest has initiated phase 1 clinical trials of TPST-1495 and TPST-1120 for the treatment of advanced solid tumors. In addition, Tempest plans to advance its TREX-1 inhibitor program and select a development candidate for this program by the end of 2021. Tempest's ability to generate product revenue will depend heavily on the successful development and eventual commercialization of TPST-1495 and TPST-1120 and Tempest's other product candidates, which may never occur. Tempest currently generates no revenue from sales of any product and Tempest may never be able to develop or commercialize a marketable product.

Each of Tempest's programs and product candidates will require further clinical and/or preclinical development, regulatory approval in multiple jurisdictions, obtaining preclinical, clinical and commercial manufacturing supply, capacity and expertise, building of a commercial organization, substantial investment and significant marketing efforts before Tempest generates any revenue from product sales. TPST-1495 and TPST-1120 and Tempest's other product candidates must be authorized for marketing by the U.S. Food and Drug Administration, or FDA, the Health Products and Food Branch of Health Canada, or HPFB, the European Medicines Agency, or EMA, and certain other foreign regulatory agencies before Tempest may commercialize any of its product candidates in the United States, Canada, EU, or other jurisdictions.

The success of TPST-1495 and TPST-1120 and Tempest's other product candidates depends on multiple factors, including:

- successful completion of preclinical studies, including those compliant with Good Laboratory Practices, or GLP, or GLP toxicology studies, biodistribution studies and minimum effective dose studies in animals, and successful enrollment and completion of clinical trials compliant with current Good Clinical Practices, or GCPs;
- effective Investigational New Drug applications, or INDs or other regulatory applications, that allow commencement of Tempest's planned clinical trials or future clinical trials for Tempest's product candidates in relevant territories;
- establishing and maintaining relationships with contract research organizations, or CROs, and clinical sites for the clinical development of Tempest's product candidates, both in the United States and internationally;
- maintenance of arrangements with third-party contract manufacturing organizations, or CMOs, for key materials used in Tempest's manufacturing processes and to establish backup sources for clinical and large-scale commercial supply;
- positive results from Tempest's clinical programs that are supportive of safety and efficacy and provide an acceptable risk-benefit profile for Tempest's product candidates in the intended patient populations;
- receipt of regulatory approvals from applicable regulatory authorities, including those necessary for pricing and reimbursement of its product candidates;
- establishment and maintenance of patent and trade secret protection and regulatory exclusivity for Tempest's product candidates;
- commercial launch of Tempest's product candidates, if and when approved, whether alone or in collaboration with others;
- acceptance of Tempest's product candidates, if and when approved, by patients, patient advocacy groups, third-party payors and the general medical community;
- Tempest's effective competition against other therapies available in the market;
- establishment and maintenance of adequate reimbursement from third-party payors for Tempest's product candidates;
- Tempest's ability to acquire or in-license additional product candidates;
- prosecution, maintenance, enforcement and defense of intellectual property rights and claims;
- maintenance of a continued acceptable safety profile of Tempest's product candidates following approval, including meeting any post-marketing commitments or requirements imposed by or agreed to with applicable regulatory authorities;
- political factors surrounding the approval process, such as government shutdowns, political instability or global pandemics such as the outbreak of the novel strain of coronavirus, COVID-19; or
- disruptions in enrollment of Tempest's clinical trials due to the COVID-19 pandemic.

If Tempest does not succeed in one or more of these factors in a timely manner or at all, Tempest could experience significant delays or an inability to successfully commercialize its product candidates, which would materially harm Tempest's business. If Tempest does not receive regulatory approvals for Tempest's product candidates, Tempest may not be able to continue its operations.

Success in preclinical studies and earlier clinical trials for Tempest's product candidates may not be indicative of the results that may be obtained in later clinical trials, which may delay or prevent obtaining regulatory approval.

Clinical development is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. Success in preclinical studies and early clinical trials may not be predictive of results in later-stage clinical trials, and successful results from early or small clinical trials may not be replicated or show as favorable an outcome in later-stage or larger clinical trials, even if successful. Tempest will be required to demonstrate through adequate and well-controlled clinical trials that Tempest's product candidates are safe and effective for their intended uses before Tempest can seek regulatory approvals for their commercial sale. The conduct of phase 3 trials and the submission of an NDA is a complicated process. Tempest has not previously completed any clinical trials, has limited experience in preparing, submitting and supporting regulatory filings, and has not previously submitted an NDA. Consequently, Tempest may be unable to successfully and efficiently execute and complete necessary clinical trials and other requirements in a way that leads to NDA submission and approval of any product candidate Tempest is developing.

Although TPST-1495 and TPST-1120 are being evaluated in clinical trials, Tempest's other product candidates, such as TREX-1, have not been evaluated in human clinical trials, and Tempest may experience unexpected or negative results in the future if and when TREX-1 or Tempest's other product candidates are evaluated in clinical trials. Any positive results Tempest observes for TREX-1 in preclinical animal models may not be predictive of Tempest's future clinical trials in humans, as animal models carry inherent limitations relevant to all preclinical studies. Tempest's product candidates, including TREX-1, may also fail to show the desired safety and efficacy in later stages of clinical development even if they successfully advance through initial clinical trials. Even if Tempest's clinical trials demonstrate acceptable safety and efficacy of TPST-1495, TPST-1120 or TREX-1 or any other product candidates and such product candidates receive regulatory approval, the labeling Tempest obtains through negotiations with the FDA or foreign regulatory authorities may not include data on secondary endpoints and may not provide Tempest with a competitive advantage over other products approved for the same or similar indications.

Many companies in the biotechnology industry have suffered significant setbacks in late-stage clinical trials after achieving positive results in early-stage development, and there is a high failure rate for product candidates proceeding through clinical trials. In addition, different methodologies, assumptions and applications Tempest utilizes to assess particular safety or efficacy parameters may yield different statistical results. Even if Tempest believes the data collected from clinical trials of Tempest's product candidates are promising, these data may not be sufficient to support approval by the FDA or foreign regulatory authorities. Preclinical and clinical data can be interpreted in different ways. Accordingly, the FDA or foreign regulatory authorities could interpret these data in different ways from Tempest or Tempest's partners, which could delay, limit or prevent regulatory approval. If Tempest's study data do not consistently or sufficiently demonstrate the safety or efficacy of any of Tempest's product candidates, including TPST-1495 and TPST-1120, to the satisfaction of the FDA or foreign regulatory authorities, then the regulatory approvals for such product candidates could be significantly delayed as Tempest works to meet approval requirements, or, if Tempest is not able to meet these requirements, such approvals could be withheld or withdrawn.

If Tempest encounters difficulties enrolling patients in Tempest's clinical trials, Tempest's clinical development activities could be delayed or otherwise adversely affected.

Tempest may experience difficulties in patient enrollment in Tempest's clinical trials for a variety of reasons, including, without limitation, the impact of the COVID-19 pandemic. The timely completion of clinical trials in accordance with their protocols depends, among other things, on Tempest's ability to enroll a sufficient number of patients who remain in the study until its conclusion. The enrollment of patients depends on many factors, including:

- the patient eligibility criteria defined in the protocol;
- the size of the patient population required for analysis of the trial's primary endpoints;
- the proximity of patients to study sites;
- the design of the trial;
- Tempest's ability to recruit clinical trial investigators with the appropriate competencies and experience;
- Tempest's ability to obtain and maintain patient consents; and
- the risk that patients enrolled in clinical trials will drop out of the trials before the infusion of Tempest's product candidates or trial completion.

Tempest intends to conduct a number of clinical trials for product candidates in the fields of cancer in geographies which are affected by COVID-19 pandemic. Tempest believes that the coronavirus pandemic could have an impact on various aspects of its future clinical trials. For example, investigators may not want to take the risk of exposing cancer patients to COVID-19 since the dosing of patients is conducted within an in-patient setting. Other potential impacts of the COVID-19 pandemic on Tempest's future various clinical trials include patient dosing and study monitoring, which may be paused or delayed due to changes in policies at various clinical sites, federal, state, local or foreign laws, rules and regulations, including quarantines or other travel restrictions, prioritization of healthcare resources toward pandemic efforts, including diminished attention of physicians serving as Tempest's clinical trial investigators and reduced availability of site staff supporting the conduct of its clinical trials, interruption or delays in the operations of the government regulators, or other reasons related to the COVID-19 pandemic. It is unknown how long these pauses or disruptions could continue.

In addition, Tempest's clinical trials will compete with other clinical trials for product candidates that are in the same therapeutic areas as Tempest's product candidates, and this competition will reduce the number and types of patients available to Tempest because some patients who might have opted to enroll in Tempest trials may instead opt to enroll in a trial being conducted by one of Tempest's competitors. Since the number of qualified clinical investigators is limited, some of Tempest's clinical trial sites are also being used by some of Tempest's competitors, which may reduce the number of patients who are available for Tempest's clinical trials in that clinical trial site.

Moreover, because Tempest's product candidates represent unproven methods for cancer treatment, potential patients and their doctors may be inclined to use existing therapies rather than enroll patients in Tempest's clinical trials.

Delays in patient enrollment may result in increased costs or may affect the timing or outcome of Tempest's ongoing clinical trial and planned clinical trials, which could prevent completion of these trials and adversely affect Tempest's ability to advance the development of Tempest's product candidates.

Interim "top line" and preliminary data from Tempest's clinical trials that Tempest may announce or publish from time to time may change as more patient data becomes available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, Tempest may publish interim "top line" or preliminary data from Tempest's clinical studies. Interim data from clinical trials that Tempest may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available.

Preliminary or "top line" data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data Tempest previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Adverse differences between preliminary or interim data and final data could significantly harm Tempest's business prospects.

Even if Tempest completes the necessary preclinical studies and clinical trials, Tempest cannot predict when, or if, Tempest will obtain regulatory approval to commercialize a product candidate and the approval may be for a narrower indication than Tempest seeks.

Prior to commercialization, TPST-1495, TPST-1120 and Tempest's other product candidates must be approved by the FDA pursuant to an NDA in the United States and pursuant to similar marketing applications by the HPFB, EMA and similar regulatory authorities outside the United States. The process of obtaining marketing approvals, both in the United States and abroad, is expensive and takes many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Failure to obtain marketing approval for a product candidate will prevent Tempest from commercializing the product candidate. Tempest has not received approval to market TPST-1495, TPST-1120 or any of Tempest's other product candidates from regulatory authorities in any jurisdiction. Tempest has no experience in submitting and supporting the applications necessary to gain marketing approvals, and, in the event regulatory authorities indicate that Tempest may submit such applications, Tempest may be unable to do so as quickly and efficiently as desired. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Tempest's product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude Tempest's obtaining marketing approval or prevent or limit commercial use. Regulatory authorities have substantial discretion in the approval process and may refuse to accept or file any application or may decide that Tempest's data are insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate.

Approval of TPST-1495 and TPST-1120 and Tempest's other product candidates may be delayed or refused for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of Tempest's clinical trials;
- Tempest may be unable to demonstrate, to the satisfaction of the FDA or comparable foreign regulatory authorities, that Tempest's product candidates are safe and effective for any of their proposed indications;
- the populations studied in clinical trials may not be sufficiently broad or representative to assure efficacy and safety in the populations for which Tempest seeks approval;
- the results of clinical trials may not meet the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- Tempest may be unable to demonstrate that Tempest's product candidates' clinical and other benefits outweigh their safety risks;
- the data collected from clinical trials of Tempest's product candidates may not be sufficient to support the submission of an NDA or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- the facilities of third-party manufacturers with which Tempest contracts or procures certain service or raw materials, may not be adequate to support approval of Tempest's product candidates; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering Tempest's clinical data insufficient for approval.

Even if Tempest's product candidates meet their pre-specified safety and efficacy endpoints in clinical trials, the regulatory authorities may not complete their review processes in a timely manner and may not consider such the clinical trial results sufficient to grant, or Tempest may not be able to obtain, regulatory approval. Additional delays may result if an FDA Advisory Committee or other regulatory authority recommends non-approval or restrictions on approval. In addition, Tempest may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory authority policy during the period of product development, clinical trials and the review process.

Regulatory authorities also may approve a product candidate for more limited indications than requested or they may impose significant limitations in the form of narrow indications, warnings, contraindications or Risk Evaluation and Mitigation Strategies, or REMS. These regulatory authorities may also grant approval subject to the performance of costly post-marketing clinical trials. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of Tempest's product candidates. Any of the foregoing scenarios could materially harm the commercial prospects for Tempest's product candidates and adversely affect Tempest's business, financial condition, results of operations and prospects.

The outbreak of COVID-19, or similar public health crises, could have a material adverse impact on Tempest's business, financial condition and results of operations, including the execution of Tempest's planned clinical trials.

In December 2019, a novel strain of coronavirus, SARS-CoV-2, was identified. This virus has since spread globally, including within the United States and while cases and hospitalization are currently on the decline in the US, there can be no assurances they will not continue at the current rate or increase in the future especially in light of the number of variants that are emerging across the world. Governments in the United States and elsewhere have taken and are continuing to take severe measures to slow the spread of COVID-19, including requiring that certain businesses close or conduct only the minimum necessary operations. The pandemic and government measures taken in response have also had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred, supply chains have been disrupted, facilities and production have been suspended, and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The extent to which COVID-19 will continue to impact Tempest's business and operating results will depend on future developments that are highly uncertain and cannot be accurately predicted, including new information that may emerge concerning COVID-19 and government measures taken in response.

Site initiation, participant recruitment and enrollment, participant dosing, distribution of clinical trial materials, study monitoring and data analysis for Tempest's planned clinical trials may be delayed due to changes in hospital or university policies, federal, state or local regulations, prioritization of hospital resources toward pandemic efforts, or other reasons related to the pandemic. Additionally, some participants and clinical investigators may not be able to comply with clinical trial protocols. For example, quarantines or other travel limitations (whether voluntary or required) may impede participant movement, affect sponsor access to study sites, or interrupt healthcare services, and Tempest may be unable to conduct its planned clinical trials. If the global effort to control the spread of COVID-19 and treat COVID-19 patients continues for an extended period of time, Tempest risks a delay in activating sites and enrolling subjects as previously projected. Any such delays to Tempest's planned clinical trials for TPST-1495 and TPST-1120 and the planned clinical trials for its other product candidates could impact the use and sufficiency of its existing cash reserves, and it may be required to raise additional capital earlier than it had previously planned. Tempest may be unable to raise additional capital if and when needed, which may result in further delays or suspension of its development plans.

Further, infections and deaths related to COVID-19 are disrupting certain healthcare and healthcare regulatory systems globally. Such disruptions could divert healthcare resources away from, or materially delay review by, the FDA and comparable foreign regulatory agencies. It is unknown how long these disruptions could continue, were they to occur. Any elongation or de-prioritization of Tempest's clinical trials or delay in regulatory review resulting from such disruptions could materially adversely affect the development and study of its product candidates.
Tempest currently utilizes third parties to, among other things, manufacture raw materials and its product candidates, components, parts, and consumables, and to perform quality testing. If either Tempest or any third-party in the supply chain for materials used in the production of its product candidates are adversely impacted by restrictions resulting from the COVID-19 pandemic, its supply chain may be disrupted, limiting Tempest's ability to manufacture product candidates for its clinical trials.

In response to the COVID-19 pandemic, Tempest complied with applicable regulation and limited required on-site staff to essential workers, with the balance of its employees continuing their work primarily outside of Tempest's offices. Due to shelter-in-place orders or other mandated local travel restrictions, third parties conducting clinical or manufacturing activities may not be able to access laboratory or manufacturing space, and Tempest's core activities may be significantly limited or curtailed, possibly for an extended period of time.

While the potential economic impact brought by and the duration of the pandemic may be difficult to assess or predict, it has already caused, and is likely to result in further, significant disruption of global financial markets and the trading prices of biopharmaceutical companies have been highly volatile as a result of the COVID-19 pandemic, which may reduce Tempest's ability to access capital either at all or on favorable terms. In addition, a recession, depression or other sustained adverse market event resulting from the global effort to control COVID-19 infections could materially and adversely affect Tempest's business.

The ultimate impact of the current pandemic, or any other health epidemic, is highly uncertain and subject to change. Tempest does not yet know the full extent of potential delays or impacts on its business, its planned clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material adverse impact on Tempest's business, financial condition and results of operations.

TPST-1495, TPST-1120 and Tempest's other product candidates may cause undesirable and/or unforeseen side effects or be perceived by the public as unsafe, which could delay or prevent their advancement into clinical trials or regulatory approval, limit the commercial potential or result in significant negative consequences.

As is the case with pharmaceuticals generally, it is likely that there may be side effects and adverse events associated with Tempest's product candidates' use. Results of Tempest's clinical trials could reveal a high and unacceptable severity and prevalence of side effects or unexpected characteristics. As Tempest continues developing its product candidates and initiate clinical trials of its additional product candidates, serious adverse events (SAEs), undesirable side effects, relapse of disease or unexpected characteristics may emerge causing Tempest to abandon these product candidates or limit their development to more narrow uses or subpopulations in which the SAEs or undesirable side effects or other characteristics are less prevalent, less severe or more acceptable from a risk-benefit perspective or in which efficacy is more pronounced or durable

If any such adverse events occur, Tempest's clinical trials could be suspended or terminated and the FDA, the HPFB, the European Commission, the EMA or other regulatory authorities could order Tempest to cease further development of, or deny approval of, Tempest's product candidates for any or all targeted indications. Even if Tempest can demonstrate that all future serious adverse events are not product-related, such occurrences could affect patient recruitment or the ability of enrolled patients to complete the trial. Moreover, if Tempest elects, or is required, to not initiate, delay, suspend or terminate any future clinical trial of any of Tempest's product candidates, the commercial prospects of such product candidates may be harmed and Tempest's ability to generate product revenues from any of these product candidates may be delayed or eliminated. Any of these occurrences may harm Tempest's ability to develop other product candidates, and may adversely affect Tempest's business, financial condition, results of operations and prospects significantly. Other treatments for cancers that utilize a dual EP2/EP4 antagonist or a PPARα antagonist or similar mechanism of action could also generate data that could adversely affect the clinical, regulatory or commercial perception of TPST-1495 and TPST-1120 and Tempest's other product candidates.

Additionally, if any of Tempest's product candidates receives marketing approval, the FDA could require Tempest to adopt a REMS to ensure that the benefits of the product outweigh its risks, which may include, for example, a Medication Guide outlining the risks of the product for distribution to patients and a communication plan to health care practitioners, or other elements to assure safe use of the product. Furthermore, if Tempest or others later identify undesirable side effects caused by Tempest's product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings in the labeling;
- Tempest may be required to change the way a product candidate is administered or conduct additional clinical trials;
- Tempest could be sued and held liable for harm caused to patients; and
- Tempest's reputation may suffer.

Any of these occurrences may harm Tempest's business, financial condition, results of operations and prospects significantly.

Tempest may not be successful in its efforts to expand its pipeline of product candidates and develop marketable products.

Because Tempest has limited financial and managerial resources, Tempest focuses on research programs and product candidates that Tempest identifies for specific indications. Tempest's business depends on its successful development and commercialization of the limited number of internal product candidates Tempest is researching or has in preclinical development. Even if Tempest is successful in continuing to build its pipeline, development of the potential product candidates that Tempest identifies will require substantial investment in additional clinical development, management of clinical, preclinical and manufacturing activities, regulatory approval in multiple jurisdictions, obtaining manufacturing supply capability, building a commercial organization, and significant marketing efforts before Tempest generates any revenue from product sales. Furthermore, such product candidates may not be suitable for clinical development, including as a result of their harmful side effects, limited efficacy or other characteristics that indicate that they are unlikely to be products that will receive marketing approval and achieve market acceptance. If Tempest cannot develop further product candidates, Tempest may not be able to obtain product revenue in future periods, which would adversely affect Tempest's business, prospects, financial condition and results of operations.

Although Tempest's pipeline includes multiple programs, Tempest is primarily focused on its lead product candidates, TPST-1495 and TPST-1120, and Tempest may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Tempest's resource allocation decisions may cause Tempest to fail to capitalize on viable commercial products or profitable market opportunities. Tempest's spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. Tempest's understanding and evaluation of biological targets for the discovery and development of new product candidates may fail to identify challenges encountered in subsequent preclinical and clinical development. If Tempest does not accurately evaluate the commercial potential or target market for a particular product candidate, Tempest may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for Tempest to retain sole development and commercialization rights.

Any product candidate for which Tempest obtains marketing approval will be subject to extensive post-marketing regulatory requirements and could be subject to post-marketing restrictions or withdrawal from the market, and Tempest may be subject to penalties if it fails to comply with regulatory requirements or if it experiences unanticipated problems with its product candidates, when and if any of them are approved.

Tempest's product candidates and the activities associated with their development and potential commercialization, including their testing, manufacturing, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, are subject to comprehensive regulation by the FDA and other U.S. and international regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements relating to manufacturing, including current Good Manufacturing Practices, or cGMPs, quality control, quality assurance and corresponding maintenance of records and documents, including periodic inspections by the FDA and other regulatory authorities and requirements regarding the distribution of samples to providers and recordkeeping. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic, unannounced inspections by the FDA and other regulatory authorities for compliance with cGMPs.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of any approved product. The FDA closely regulates the post-approval marketing and promotion of drugs to ensure that they are marketed in a manner consistent with the provisions of the approved labeling. The FDA imposes stringent restrictions on manufacturers' communications regarding use of their products. If Tempest promotes its product candidates in a manner inconsistent with FDA-approved labeling or otherwise not in compliance with FDA regulations, Tempest may be subject to enforcement action. Violations of the Federal Food, Drug, and Cosmetic Act relating to the promotion of prescription drugs may lead to investigations alleging violations of federal and state healthcare fraud and abuse laws, as well as state consumer protection laws and similar laws in international jurisdictions.

In addition, later discovery of previously unknown adverse events or other problems with Tempest's product candidates, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may yield various results, including:

- restrictions on such product candidates, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of any approved product from the market;
- refusal to approve pending applications or supplements to approved applications that Tempest submits;
- recall of product candidates;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- refusal to permit the import or export of Tempest's product candidates;
- product seizure; or
- injunctions or the imposition of civil or criminal penalties.

The occurrence of any event or penalty described above may inhibit Tempest's ability to commercialize its product candidates and generate revenue and could require Tempest to expend significant time and resources in response and could generate negative publicity. The FDA's and other regulatory authorities' policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of Tempest's product candidates. If Tempest is slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if Tempest is not able to maintain regulatory compliance, it may lose any marketing approval that it has obtained, and Tempest may not achieve or sustain profitability.

Non-compliance with Canadian and European requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with Canada's or Europe's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Tempest's failure to obtain regulatory approval in international jurisdictions would prevent Tempest from marketing its product candidates outside the United States.

To market and sell TPST-1495, TPST-1120 and Tempest's other product candidates in other jurisdictions, Tempest must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time and data required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, Tempest must secure product reimbursement approvals before regulatory authorities will approve the product for sale in that country. Failure to obtain foreign regulatory approvals or non-compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for Tempest and could delay or prevent the introduction of Tempest's product candidates in certain countries.

If Tempest fails to comply with the regulatory requirements in international markets and receive applicable marketing approvals, Tempest's target market will be reduced and its ability to realize the full market potential of its product candidates will be harmed and its business will be adversely affected. Tempest may not obtain foreign regulatory approvals on a timely basis, if at all. Tempest's failure to obtain approval of any of its product candidates by regulatory authorities in another country may significantly diminish the commercial prospects of that product candidate and Tempest's business prospects could decline.

Risks Related to Commercialization and Manufacturing

The commercial success of Tempest's product candidates, including TPST-1495 and TPST-1120, will depend upon their degree of market acceptance by providers, patients, patient advocacy groups, third-party payors and the general medical community.

Even if the requisite approvals from the FDA, the HPFB, the EMA and other regulatory authorities internationally are obtained, the commercial success of Tempest's product candidates will depend, in part, on the acceptance of providers, patients and third-party payors of drugs designed to act as a dual antagonist of EP2 and EP4 and PPARα antagonists in general, and Tempest's product candidates in particular, as medically necessary, cost-effective and safe. In addition, Tempest may face challenges in seeking to establish and grow sales of TPST-1495 and TPST-1120 or its other product candidates. Any product that Tempest commercializes may not gain acceptance by providers, patients, patient advocacy groups, third-party payors and the general medical community. If these products do not achieve an adequate level of acceptance, Tempest may not generate significant product revenue and may not become profitable. The degree of market acceptance of TPST-1495, TPST-1120 and Tempest's other product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy, durability and safety of such product candidates as demonstrated in clinical trials;
- the potential and perceived advantages of product candidates over alternative treatments;
- the cost of treatment relative to alternative treatments;
- the clinical indications for which the product candidate is approved by the FDA, the HPFB or the European Commission;
- the willingness of providers to prescribe new therapies;
- the willingness of the target patient population to try new therapies;
- the prevalence and severity of any side effects;
- product labeling or product insert requirements of the FDA, the HPFB, EMA or other regulatory authorities, including any limitations or warnings contained in a product's approved labeling;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the quality of Tempest's relationships with patient advocacy groups;
- publicity concerning Tempest's product candidates or competing products and treatments; and
- sufficient third-party payor coverage and adequate reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be fully known until after it is launched.

The pricing, insurance coverage and reimbursement status of newly approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for Tempest's product candidates, if approved, could limit Tempest's ability to market those products and decrease Tempest's ability to generate product revenue.

Successful sales of Tempest's product candidates, if approved, depend on the availability of coverage and adequate reimbursement from third-party payors including governmental healthcare programs, such as Medicare and Medicaid, managed care organizations and commercial payors, among others. Significant uncertainty exists as to the coverage and reimbursement status of any product candidates for which Tempest obtains regulatory approval. In addition, because Tempest's product candidates represent new approaches to the treatment of cancer, Tempest cannot accurately estimate the potential revenue from Tempest's product candidates.

Tempest expects that coverage and reimbursement by third-party payors will be essential for most patients to be able to afford these treatments. Accordingly, sales of Tempest's product candidates will depend substantially, both domestically and internationally, on the extent to which the costs of Tempest's product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or will be reimbursed by government payors, private health coverage insurers and other third-party payors. Even if coverage is provided, the established reimbursement amount may not be high enough to allow Tempest to establish or maintain pricing sufficient to realize a sufficient return on Tempest's investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, third-party payors, including private and governmental payors, such as the Medicare and Medicaid programs, play an important role in determining the extent to which new drugs will be covered and reimbursed. The Medicare program covers certain individuals aged 65 or older, disabled or suffering from end-stage renal disease. The Medicaid program, which varies from state-to-state, covers certain individuals and families who have limited financial means. The Medicare and Medicaid programs increasingly are used as models for how private payors and other government payors develop their coverage and reimbursement policies for drugs. One payor's determination to provide coverage for a drug product, however, does not assure that other payors will also provide coverage for the drug product. Further, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved.

In addition to government and private payors, professional organizations such as the American Medical Association, or the AMA, can influence decisions about coverage and reimbursement for new products by determining standards for care. In addition, many private payors contract with commercial vendors who sell software that provide guidelines that attempt to limit utilization of, and therefore reimbursement for, certain products deemed to provide limited benefit compared to existing alternatives. Such organizations may set guidelines that limit reimbursement or utilization of Tempest's product candidates, if approved. Even if favorable coverage and reimbursement status is attained for one or more product candidates for which Tempest's collaborators receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and Tempest believes the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries has and will continue to put pressure on the pricing and usage of therapeutics such as Tempest's product candidates. In many countries, particularly the countries of the EU, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, Tempest may be required to conduct a clinical trial that compares the cost-effectiveness of Tempest's product candidate to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that Tempest is able to charge for its product candidates. Accordingly, in markets outside the United States, the reimbursement for Tempest's product candidates may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by government and other third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such payors to limit both coverage and the level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for Tempest's product candidates. Tempest expects to experience pricing pressures in connection with the sale of any of Tempest's product candidates due to the trend toward managed healthcare, the increasing influence of certain third-party payors, such as health maintenance organizations, and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market. Recently there have been instances in which third-party payors have refused to reimburse treatments for patients for whom the treatment is indicated in the FDA-approved product labeling. Even if Tempest is successful in obtaining FDA approval to commercialize Tempest's product candidates, Tempest cannot guarantee that Tempest will be able to secure reimbursement for all patients for whom treatment with Tempest's product candidates is indicated.

If third parties on which Tempest depends to conduct its planned preclinical studies or clinical trials do not perform as contractually required, fail to satisfy regulatory or legal requirements or miss expected deadlines, Tempest's development program could be delayed with adverse effects on Tempest's business, financial condition, results of operations and prospects.

Tempest relies on third party CROs, CMOs, consultants and others to design, conduct, supervise and monitor key activities relating to, discovery, manufacturing, preclinical studies and clinical trials of Tempest's product candidates, and Tempest intends to do the same for future activities relating to existing and future programs. Because Tempest relies on third parties and does not have the ability to conduct all required testing, discovery, manufacturing, preclinical studies or clinical trials independently, Tempest has less control over the timing, quality and other aspects of discovery, manufacturing, preclinical studies and clinical trials than Tempest would if Tempest conducted them on its own. These investigators, CROs, CMOs and consultants are not Tempest's employees, and Tempest has limited control over the amount of time and resources that they dedicate to Tempest's programs. These third parties may have contractual relationships with other entities, some of which may be Tempest's competitors, which may draw time and resources from Tempest's programs. The third parties Tempest contracts with might not be diligent, careful or timely in conducting Tempest's discovery, manufacturing, preclinical studies or clinical trials, resulting in testing, discovery, manufacturing, preclinical studies or clinical trials being delayed or unsuccessful, in whole or in part.

If Tempest cannot contract with acceptable third parties on commercially reasonable terms, or at all, or if these third parties do not carry out their contractual duties, satisfy legal and regulatory requirements for the conduct of preclinical studies or clinical trials or meet expected deadlines, Tempest's clinical development programs could be delayed and otherwise adversely affected. In all events, Tempest is responsible for ensuring that each of Tempest's preclinical studies and clinical trials is conducted in accordance with the general investigational plan and protocols for the trial, as well as in accordance with GLP, GCP and other applicable laws, regulations and standards. Tempest's reliance on third parties that it does not control does not relieve Tempest of these responsibilities and requirements. The FDA and other regulatory authorities enforce GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If Tempest or any of these third parties fails to comply with applicable GCPs, the clinical data generated in its clinical trials may be deemed unreliable and the FDA or comparable foreign regulatory authorities may require Tempest to perform additional clinical trials before approving its marketing applications. Tempest cannot assure you that upon inspection by a given regulatory authority, such regulatory authority will determine that any of Tempest's clinical trials have complied with GCPs. In addition, Tempest's clinical trials must be conducted with product produced in accordance with cGMPs. Tempest's failure to comply with these regulations may require it to repeat clinical trials, which could delay or prevent the receipt of regulatory approvals. Any such event could have an adverse effect on Tempest's business, financial condition, results of operations and prospects.

Tempest faces significant competition in an environment of rapid technological change, and it is possible that Tempest's competitors may achieve regulatory approval before Tempest or develop therapies that are more advanced or effective than Tempest's, which may harm Tempest's business, financial condition and Tempest's ability to successfully market or commercialize TPST-1495, TPST-1120, and Tempest's other product candidates.

The biopharmaceutical industry, and the immuno-oncology industry specifically, is characterized by intense competition and rapid innovation. Tempest is aware of other companies focused on developing cancer therapies in various indications. Tempest may also face competition from large and specialty pharmaceutical and biotechnology companies, academic research institutions, government agencies and public and private research institutions that conduct research, seek patent protection, and establish collaborative arrangements for research, development, manufacturing and commercialization.

Many of Tempest's potential competitors, alone or with their strategic partners, may have substantially greater financial, technical and other resources than Tempest does, such as larger research and development, clinical, marketing and manufacturing organizations. Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of competitors. Tempest's commercial opportunity could be reduced or eliminated if competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product candidates that Tempest may develop. Competitors also may obtain FDA or other regulatory approval for their products more rapidly than Tempest may obtain approval for its products, which could result in Tempest's competitors establishing a strong market position before Tempest is able to enter the market, if ever. Additionally, new or advanced technologies developed by Tempest's competitors may render Tempest's current or future product candidates uneconomical or obsolete, and Tempest may not be successful in marketing its product candidates against competitors.

To become and remain profitable, Tempest must develop and eventually commercialize product candidates with significant market potential, which will require Tempest to be successful in a range of challenging activities.

These activities include, among other things, completing preclinical studies and initiating and completing clinical trials of Tempest's product candidates, obtaining marketing approval for these product candidates, manufacturing, marketing and selling those products that are approved and satisfying any post marketing requirements. Tempest may never succeed in any or all of these activities and, even if Tempest does, Tempest may never generate revenues that are significant or large enough to achieve profitability. If Tempest does achieve profitability, Tempest may not be able to sustain or increase profitability on a quarterly or annual basis. Tempest's failure to become and remain profitable would decrease the value of Tempest and could impair Tempest's ability to raise capital, maintain Tempest's research and development efforts, expand Tempest's business or continue operations. A decline in the value of Tempest also could cause you to lose all or part of your investment.

Tempest may rely on third parties to manufacture Tempest's clinical product supplies, and Tempest may have to rely on third parties to produce and process Tempest's product candidates, if approved.

Tempest must currently rely on outside vendors to manufacture supplies and process Tempest's product candidates. Tempest has not yet caused its product candidates to be manufactured or processed on a commercial scale and may not be able to achieve manufacturing and processing and may be unable to create an inventory of mass-produced, off-the-shelf product to satisfy demands for any of Tempest's product candidates.

Tempest does not yet have sufficient information to reliably estimate the cost of the commercial manufacturing and processing of Tempest's product candidates, and the actual cost to manufacture and process Tempest's product candidates could materially and adversely affect the commercial viability of its product candidates. As a result, Tempest may never be able to develop a commercially viable product.

In addition, Tempest anticipates reliance on a limited number of third-party manufacturers exposes it to the following risks:

- Tempest may be unable to identify manufacturers on acceptable terms or at all because the number of potential manufacturers is limited, and the FDA may have questions regarding any replacement contractor. This may require new testing and regulatory interactions. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of Tempest's products after receipt of FDA questions, if any.
- Tempest's third-party manufacturers might be unable to timely formulate and manufacture Tempest's product or produce the quantity and quality required to meet Tempest's clinical and commercial needs, if any.
- Contract manufacturers may not be able to execute Tempest's manufacturing procedures appropriately.

- Tempest's future contract manufacturers may not perform as agreed or may not remain in the contract manufacturing business for the time required to supply Tempest's clinical trials or to successfully produce, store and distribute Tempest's products.
- Manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the Drug Enforcement Administration and corresponding state agencies to ensure strict compliance with cGMP and other government regulations and corresponding foreign standards. Tempest does not have control over third-party manufacturers' compliance with these regulations and standards.
- Tempest may not own, or may have to share, the intellectual property rights to any improvements made by Tempest's third-party manufacturers in the manufacturing process for Tempest's products.
- Tempest's third-party manufacturers could breach or terminate their agreement(s) with Tempest.

Tempest's contract manufacturers would also be subject to the same risks Tempest faces in developing its own manufacturing capabilities, as described above. Each of these risks could delay Tempest's clinical trials, the approval, if any, of Tempest's product candidates by the FDA or the commercialization of Tempest's product candidates or result in higher costs or deprive Tempest of potential product revenue. In addition, Tempest will rely on third parties to perform release tests on Tempest's product candidates prior to delivery to patients. If these tests are not appropriately done and test data are not reliable, patients could be put at risk of serious harm.

The manufacture of drugs is complex, and Tempest's third-party manufacturers may encounter difficulties in production. If any of Tempest's third-party manufacturers encounter such difficulties, Tempest's ability to provide adequate supply of its product candidates for clinical trials, Tempest's ability to obtain marketing approval, or Tempest's ability to provide supply of Tempest's product candidates for patients, if approved, could be delayed or stopped.

Tempest intends to establish manufacturing relationships with a limited number of suppliers to manufacture raw materials, the drug substance and finished product of any product candidate for which Tempest is responsible for preclinical or clinical development. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain. As part of any marketing approval, a manufacturer and its processes are required to be qualified by the FDA prior to regulatory approval. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in Tempest's desired clinical and commercial timelines.

The process of manufacturing drugs is complex, highly-regulated and subject to multiple risks. Manufacturing drugs is highly susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment, vendor or operator error, inconsistency in yields, variability in product characteristics and difficulties in scaling the production process. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered at the facilities of Tempest's manufacturers, such facilities may need to be closed for an extended period of time to investigate and remedy the contamination, which could delay clinical trials and adversely harm Tempest's business. Moreover, if the FDA determines that Tempest's CMOs are not in compliance with FDA laws and regulations, including those governing cGMPs, the FDA may deny NDA approval until the deficiencies are corrected or Tempest replaces the manufacturer in Tempest's NDA with a manufacturer that is in compliance. In addition, approved products and the facilities at which they are manufactured are required to maintain ongoing compliance with extensive FDA requirements and the requirements of other similar agencies, including ensuring that quality control and manufacturing procedures conform to cGMP requirements. As such, Tempest's CMOs are subject to continual review and periodic inspections to assess compliance with cGMPs. Furthermore, although Tempest does not have day-to-day control over the operations of its CMOs, it is responsible for ensuring compliance with applicable laws and regulations, including cGMPs.

In addition, there are risks associated with large scale manufacturing for clinical trials or commercial scale including, among others, cost overruns, potential problems with process scale-up, process reproducibility, stability issues, compliance with good manufacturing practices, lot consistency and timely availability of raw materials. Even if Tempest's collaborators obtain regulatory approval for any of Tempest's product candidates, there is no assurance that manufacturers will be able to manufacture the approved product to specifications acceptable to the FDA or other regulatory authorities, to produce it in sufficient quantities to meet the requirements for the potential launch of the product or to meet potential future demand. If Tempest's manufacturers are unable to produce sufficient quantities for clinical trials or for commercialization, commercialization efforts would be impaired, which would have an adverse effect on Tempest's business, financial condition, results of operations and prospects.

Tempest believes that it will rely upon on a limited number of manufacturers for its product candidates, which may include single-source suppliers for the various steps of manufacture. This reliance on a limited number of manufacturers and the complexity of drug manufacturing and the difficulty of scaling up a manufacturing process could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of Tempest's product candidates, cause Tempest to incur higher costs and prevent Tempest from commercializing Tempest's product candidates successfully. Furthermore, if Tempest's suppliers fail to deliver the required commercial quantities of materials on a timely basis and at commercially reasonable prices, and Tempest is unable to secure one or more replacement suppliers capable of production in a timely manner at a substantially equivalent cost, Tempest's clinical trials may be delayed or Tempest could lose potential revenue.

If Tempest is unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell Tempest's product candidates, Tempest may be unable to generate any revenues.

Tempest currently does not have an organization for the sales, marketing and distribution of TPST-1495, TPST-1120, TREX-1 and Tempest's other product candidates, and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. To market any products that may be approved, Tempest must build its sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. With respect to certain of Tempest's current programs as well as future programs, Tempest may rely completely on an alliance partner for sales and marketing. In addition, although Tempest intends to establish a sales organization if Tempest is able to obtain approval to market any product candidates, Tempest may enter into strategic alliances with third parties to develop and commercialize TPST-1495, TPST-1120 and other product candidates, including in markets outside of the United States or for other large markets that are beyond Tempest's resources. This will reduce the revenue generated from the sales of these products.

Any future strategic alliance partners may not dedicate sufficient resources to the commercialization of Tempest's product candidates or may otherwise fail in their commercialization due to factors beyond Tempest's control. If Tempest is unable to establish effective alliances to enable the sale of Tempest's product candidates to healthcare professionals and in geographical regions, including the United States, that will not be covered by Tempest's marketing and sales force, or if Tempest's potential future strategic alliance partners do not successfully commercialize the product candidates, Tempest's ability to generate revenues from product sales will be adversely affected.

If Tempest is unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, Tempest may not be able to generate sufficient product revenue and may not become profitable. Tempest will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, Tempest may be unable to compete successfully against these more established companies.

Tempest may not be successful in finding strategic collaborators for continuing development of certain of Tempest's future product candidates or successfully commercializing or competing in the market for certain indications.

In the future, Tempest may decide to collaborate with non-profit organizations, universities and pharmaceutical and biotechnology companies for the development and potential commercialization of existing and new product candidates. Tempest faces significant competition in seeking appropriate collaborators. Whether Tempest reaches a definitive agreement for a collaboration will depend, among other things, upon Tempest's assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing drugs, the existence of uncertainty with respect to Tempest's ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with Tempest for Tempest's product candidate. The terms of any additional collaborations or other arrangements that Tempest may establish may not be favorable to Tempest. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators.

Tempest may not be able to negotiate collaborations on a timely basis, on acceptable terms, or at all. If Tempest is unable to do so, Tempest may have to curtail the development of the product candidate for which Tempest is seeking to collaborate, reduce or delay its development program or one or more of Tempest's other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase Tempest's expenditures and undertake development or commercialization activities at Tempest's expense. If Tempest elects to increase Tempest's expenditures to fund development or commercialization activities on Tempest's product candidates, Tempest may need to obtain additional capital, which may not be available to Tempest on acceptable terms or at all. If Tempest does not have sufficient funds, Tempest may not be able to further develop Tempest's product candidates or bring them to market and generate product revenue.

The success of any potential collaboration arrangements will depend heavily on the efforts and activities of Tempest's collaborators. Collaborators generally have significant discretion in determining the efforts and resources that they will apply to these collaborations. Disagreements between parties to a collaboration arrangement regarding clinical development and commercialization matters can lead to delays in the development process or commercializing the applicable product candidate and, in some cases, termination of such collaboration arrangements. These disagreements can be difficult to resolve if neither of the parties has final decision-making authority. Collaborations with pharmaceutical or biotechnology companies and other third parties often are terminated or allowed to expire by the other party. Any such termination or expiration would adversely affect Tempest financially and could harm Tempest's business reputation.

Risks Related to Government Regulation

The FDA regulatory approval process is lengthy and time-consuming, and Tempest may experience significant delays in the clinical development and regulatory approval of Tempest's product candidates.

Obtaining FDA approval is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the type, complexity and novelty of the product candidates involved. In addition, approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, which may cause delays in the approval or the decision not to approve an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that Tempest's data are insufficient for approval and require additional preclinical, clinical or other data. Even if Tempest eventually completes clinical testing and receive approval for its product candidates, the FDA may approve its product candidates for a more limited indication or a narrower patient population than originally requested or may impose other prescribing limitations or warnings that limit the product's commercial potential. Tempest has not submitted for, or obtained, regulatory approval for any product candidate, and it is possible that none of its product candidates will ever obtain regulatory approval. Further, development of Tempest's product candidates and/or regulatory approval may be delayed for reasons beyond its control.

Tempest may also experience delays in obtaining regulatory approvals, including but not limited to:

- obtaining regulatory authorization to begin a trial, if applicable;
- redesigning its study protocols and need to conduct additional studies as may be required by a regulator;
- governmental or regulatory delays and changes in regulation or policy relating to the development and commercialization of its product candidate by the FDA or other comparable foreign regulatory authorities;

- the outcome, timing and cost of meeting regulatory requirements established by the FDA, and other comparable foreign regulatory authorities;
- the availability of financial resources to commence and complete the planned trials;
- negotiating the terms of any collaboration agreements Tempest may choose to initiate or conclude;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- failure of third-party contractors, such as CROs, or investigators to comply with regulatory requirements, including good clinical practice standards (GCPs);
- clinical sites deviating from trial protocol or dropping out of a trial;
- delay or failure in obtaining the necessary approvals from regulators or institutional review boards, or IRBs, in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;
- Inability to recruit and enroll suitable patients to participate in a trial;
- having patients complete a trial, including having patients enrolled in clinical trials dropping out of the trial before the product candidate is manufactured and returned to the site, or return for post-treatment follow-up;
- difficulty in having patients complete a trial or return for post-treatment follow-up;
- clinical trial sites deviating from trial protocol or dropping out of a trial;
- addressing any patient safety concerns that arise during the course of a trial;
- inability to add new clinical trial sites; or
- varying interpretations of the data generated from its preclinical or clinical trials;
- the cost of defending intellectual property disputes, including patent infringement actions brought by third parties;
- the effect of competing technological and market developments;
- the cost and timing of establishing, expanding and scaling manufacturing capabilities;
- inability to manufacture, or obtain from third parties, sufficient quantities of qualified materials under cGMPs, for the completion in pre-clinical and clinical studies;
- problems with biopharmaceutical product candidate storage, stability and distribution resulting in global supply chain disruptions;
- the cost of establishing sales, marketing and distribution capabilities for any product candidate for which Tempest may receive regulatory approval in regions where Tempest chooses to commercialize its products on its own; or
- potential unforeseen business disruptions or market fluctuations that delay its product development or clinical trials and increase its costs or expenses, such as business or operational disruptions, delays, or system failures due to malware, unauthorized access, terrorism, war, natural disasters, strikes, geopolitical conflicts, restrictions on trade, import or export restrictions, or public health crises, such as the current COVID-19 pandemic.

Tempest could also encounter delays if physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of Tempest's product candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by Tempest, the IRBs for the institutions in which such trials are being conducted or by the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or Tempest clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, safety issues or adverse side effects, failure to demonstrate a benefit from using a product candidate, changes in governmental regulations or administrative actions, lack of adequate funding to continue the clinical trial, or based on a recommendation by the Data Safety Monitoring Committee. If Tempest experiences termination of, or delays in the completion of, any clinical trial of Tempest's product candidates, the commercial prospects for Tempest's product candidates will be harmed, and Tempest's ability to generate product revenue will be delayed. In addition, any delays in completing Tempest's clinical trials will increase Tempest's costs, slow down Tempest's product development and approval process and jeopardize Tempest's ability to commence product sales and generate revenue.

Many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may ultimately lead to the denial of regulatory approval of Tempest's product candidates.

Tempest may seek Breakthrough Therapy designation or Fast Track designation by the FDA for one or more of its product candidates, but may not receive such designation. Even if Tempest secures such designation, it may not lead to a faster development or regulatory review or approval process and it does not increase the likelihood that Tempest's product candidates will receive marketing approval.

Tempest may seek Breakthrough Therapy or Fast Track designation for some of its product candidates. If a product candidate is intended for the treatment of a serious or life-threatening condition and clinical or preclinical data demonstrate the potential to address unmet medical needs for this condition, the product candidate may be eligible for Fast Track designation. The benefits of Fast Track designation include more frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval, more frequent written communication from FDA about such things as the design of the proposed clinical trials and use of biomarkers, eligibility for Accelerated Approval and Priority Review, if relevant criteria are met, and rolling review, which means that a drug company can submit completed sections of its NDA for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be reviewed. NDA review usually does not begin until the entire application has been submitted to the FDA.

A breakthrough therapy is defined as a drug that is intended, alone or in combination with one or more other drugs or biologics, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. Drugs designated as breakthrough therapies by the FDA may be eligible for all features of Fast Track designation, intensive guidance on an efficient drug development program, beginning as early as Phase 1, and organizational commitment involving senior managers at FDA.

The FDA has broad discretion whether or not to grant these designations, so even if Tempest believes a particular product candidate is eligible, it cannot assure that the FDA would decide to grant the designation. Even if Tempest obtains Fast Track designation and/or Breakthrough Therapy designation for one or more of Tempest's product candidates, it may not experience a faster development process, review or approval compared to non-expedited FDA review procedures. In addition, the FDA may withdraw Fast Track designation or Breakthrough Therapy designation if it believes that the designation is no longer supported. These designations do not guarantee qualification for the FDA's priority review procedures or a faster review or approval process.

Tempest may attempt to secure FDA approval of its product candidates through the accelerated approval pathway. If Tempest is unable to obtain accelerated approval, Tempest may be required to conduct additional preclinical studies or clinical trials beyond those that Tempest currently contemplates, which could increase the expense of obtaining, and delay the receipt of, necessary marketing approvals.

Tempest is developing certain product candidates for the treatment of serious conditions, and therefore may decide to seek approval of such product candidates under the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it is designed to treat a serious or life-threatening disease or condition and provides a meaningful therapeutic benefit over existing treatments based upon a determination that the product candidate has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability of or lack of alternative treatments. For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit.

The accelerated approval pathway may be used in cases in which the advantage of a new drug over available therapy may not be a direct therapeutic advantage, but is a clinically important improvement from a patient and public health perspective. If granted, accelerated approval is usually contingent on the sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verity and describe the drug's anticipated effect on irreversible morbidity or mortality or other clinical benefit. In some cases, the FDA may require that the trial be designed, initiated, and/or fully enrolled prior to approval. If the sponsor fails to conduct such studies in a timely manner, or if such post-approval studies fail to verify the drug's predicted clinical benefit, or if other evidence demonstrates that Tempest's product candidate is not shown to be safe and effective under the conditions of use, the FDA may withdraw its approval of the drug on an expedited basis.

If Tempest decides to submit an NDA seeking accelerated approval or receives an expedited regulatory designation for any of its product candidates, there can be no assurance that such submission or application will be accepted or that any expedited development, review or approval will be granted on a timely basis, or at all. If any of Tempest's competitors were to receive full approval on the basis of a confirmatory trial for an indication for which Tempest is seeking accelerated approval before Tempest receives accelerated approval, the indication Tempest is seeking may no longer qualify as a condition for which there is an unmet medical need and accelerated approval of its product candidate would be more difficult or may not occur.

Failure to obtain accelerated approval or any other form of expedited development, review or approval for Tempest's product candidates would result in a longer time period to commercialization of such product candidate, if any, and could increase the cost of development of such product candidate harm Tempest's competitive position in the marketplace.

Tempest may be unsuccessful in obtaining Orphan Drug Designation for its product candidates or transfer of designations obtained by others for future product candidates, and, even if Tempest obtains such designation, it may be unable to maintain the benefits associated with Orphan Drug Designation, including the potential for market exclusivity.

FDA may designate drugs intended to treat relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a drug as an orphan drug if it is intended to treat a rare disease or condition, which is defined as a patient population of fewer than 200,000 individuals in the United States, or a patient population greater than 200,000 in the United States when there is no reasonable expectation that the cost of developing and making available the drug in the United States will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. In the United States, Orphan Drug Designation entitles a party to financial incentives such as opportunities for tax credits for qualified clinical research costs and exemption from prescription drug user fees. Generally, if a drug with an Orphan Drug Designation subsequently receives the first marketing approval for the indication for which it has such designation, the drug is entitled to a period of marketing exclusivity, which precludes FDA from approving another marketing application for the same drug and indication for that time period, except in limited circumstances. If a competitor is able to obtain orphan drug exclusivity prior to Tempest for a product that constitutes the same active moiety and treats the same indications as Tempest's product candidates, Tempest may not be able to obtain approval of its drug by the applicable regulatory authority for a significant period of time unless Tempest is able to show that its drug is clinically superior to the approved drug. The applicable period is seven years in the United States.

Tempest may seek Orphan Drug Designation for one or more of its product candidates in the United States as part of its business strategy. However, Orphan Drug Designation does not guarantee future orphan drug marketing exclusivity. Even after an orphan drug is approved, the FDA can also subsequently approve a later application for the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer in a substantial portion of the target populations, more effective or makes a major contribution to patient care. In addition, a designated orphan drug may not receive orphan drug exclusivity if it is approved for a use that is broader than the indication for which it received orphan designation. Moreover, orphan drug exclusive marketing rights in the United States may be lost if the FDA later determines that the request for designation was materially defective or if Tempest is unable to manufacture sufficient quantities of the product to meet the needs of patients with the rare disease or condition. Orphan Drug Designation neither shortens the development time or regulatory review time of a drug nor gives the drug any advantage in the regulatory review or approval process.

Enacted and future legislation may increase the difficulty and cost for Tempest to commercialize and obtain marketing approval of Tempest's product candidates and may affect the prices Tempest may set.

Existing regulatory policies may change, and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of Tempest's product candidates. Tempest cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If Tempest is slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if Tempest is not able to maintain regulatory compliance, Tempest may lose any marketing approval that Tempest may have obtained, and Tempest may not achieve or sustain profitability.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the Affordable Care Act, or ACA, was enacted to broaden access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The ACA contains provisions that may potentially affect the profitability of Tempest's product candidates, if approved, including, for example, increased rebates for products sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs, and expansion of the entities eligible for discounts under the 340B Drug Pricing Program.

While Congress has not passed legislation to comprehensively repeal the ACA, legislation affecting the ACA has been signed into law, including the Tax Cuts and Jobs Act of 2017, which eliminated, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year, which is commonly referred to as the "individual mandate." On June 17, 2021, the U.S. Supreme Court dismissed the most recent judicial challenge to the ACA brough by several states without specifically ruling on the constitutionality of the law. While Congress continues to amend the ACA, the law appears likely to continue the downward pressure on pharmaceutical pricing, and may also increase Tempest's regulatory burdens and operating costs. In the future, there may be other efforts to challenge, repeal or replace the ACA. Tempest is continuing to monitor any changes to the ACA that, in turn, may potentially impact its business in the future.

Additionally, on May 30, 2018, the Trickett Wendler, Frank Mongiello, Jordan McLinn and Matthew Bellina Right to Try Act of 2017 was signed into law. The law, among other things, provides a federal framework for certain patients who have been diagnosed with life-threatening diseases or conditions to access certain investigational new drug products that have completed a phase 1 clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA authorization under an FDA expanded access program; however, manufacturers are not obligated to provide investigational new drug products under the current federal right to try law. Tempest may choose to seek an expanded access program for Tempest's product candidates, or to utilize comparable rules in other countries that allow the use of a drug, on a named patient basis or under a compassionate use program.

Recently, the cost of prescription pharmaceuticals has been the subject of considerable discussion in the United States at both the federal and state levels. While several proposed reform measures will require Congress to pass legislation to become effective, Congress and the new Biden administration have each indicated that it will seek new legislative and/or administrative measures to address prescription drug costs. Since the Presidential inauguration, the Biden administration has taken several executive actions that signal changes in policy from the prior administration. For example, on July 9, 2021, President Biden signed an executive order to promote competition in the U.S. economy that included several initiatives aimed prescription drugs. Among other provisions, the executive order directed the Secretary of HHS to issue a report to the White House within 45 days that includes a plan to, among other things, reduce prices for prescription drugs, including prices paid by the federal government for such drugs. At the state level, legislatures and agencies are increasingly passing legislation and implementing regulations designed to control spending on and patient out-of-pocket costs for drug products. These measures include constraints on pricing, discounting and reimbursement; restrictions on certain product access and marketing; cost disclosure and transparency measures that require detailed reporting of drug pricing and marketing information both at product launch and in the event of a price increase; and, in some cases, measures designed to encourage importation from other countries and bulk purchasing.

Tempest expects that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that Tempest receives for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent Tempest from being able to generate revenue, attain profitability, or commercialize Tempest's product candidates.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. Tempest cannot be sure whether additional legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of Tempest's product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject Tempest to more stringent product labeling and post-marketing testing and other requirements.

The FDA's ability to review and approve new products may be hindered by a variety of factors, including budget and funding levels, ability to hire and retain key personnel, statutory, regulatory and policy changes and global health concerns.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, statutory, regulatory and policy changes, the FDA's ability to hire and retain key personnel and accept the payment of user fees, and other events that may otherwise affect the FDA's ability to perform routine functions. In addition, government funding of other government agencies that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable. Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect Tempest's business. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA, have had to furlough critical employees and stop critical activities.

The ability of the FDA and other government agencies to properly administer their functions is highly dependent on the levels of government funding and the ability to fill key leadership appointments, among various factors. Delays in filling or replacing key positions could significantly impact the ability of the FDA and other agencies to fulfill their functions, and could greatly impact healthcare and the pharmaceutical industry.

Separately, in response to the COVID-19 pandemic, on March 10, 2020, the FDA announced its intention to postpone most foreign inspections of manufacturing facilities and, subsequently, on March 18, 2020, the FDA temporarily postponed routine surveillance inspections of domestic manufacturing facilities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. Subsequently, on July 10, 2020 the FDA announced its intention to resume certain on-site inspections of domestic manufacturing facilities subject to a risk-based prioritization system. The FDA intends to use this risk-based assessment system to identify the categories of regulatory activity that can occur within a given geographic area, ranging from mission critical inspections to resumption of all regulatory activities. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic. If a prolonged government shutdown occurs, or if global health concerns continue to prevent the FDA or other regulatory authorities from conducting their regular inspections, reviews, or other regulatory activities, it could significantly impact the ability of the FDA or other regulatory authorities to timely review and process Tempest's regulatory submissions, which could have a material adverse effect on Tempest's business.

Obtaining and maintaining regulatory approval of Tempest's product candidates in one jurisdiction does not mean that Tempest will be successful in obtaining regulatory approval of Tempest's product candidates in other jurisdictions.

Obtaining and maintaining regulatory approval of Tempest's product candidates in one jurisdiction does not guarantee that Tempest will be able to obtain or maintain regulatory approval in any other jurisdiction, while a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory approval process in others. For example, even if the FDA grants marketing approval of a product candidate, comparable regulatory authorities in foreign jurisdictions must also approve the manufacturing, marketing and promotion of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials as clinical studies conducted in one jurisdiction may not be accepted by regulatory authorities in other jurisdictions. In many jurisdictions outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that jurisdiction. In some cases, the price that Tempest intends to charge for Tempest's products is also subject to approval.

Tempest may also submit marketing applications in other countries. Regulatory authorities in jurisdictions outside of the United States have requirements for approval of product candidates with which Tempest must comply prior to marketing in those jurisdictions. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for Tempest and could delay or prevent the introduction of Tempest's products in certain countries. If Tempest fails to comply with the regulatory requirements in international markets and/or receive applicable marketing approvals, Tempest's target market will be reduced and Tempest's ability to realize the full market potential of Tempest's product candidates will be harmed.

Tempest's operations and relationships with future customers, providers and third-party payors will be subject to applicable anti-kickback, fraud and abuse and other healthcare laws and regulations, which could expose Tempest to penalties including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

Healthcare providers and third-party payors will play a primary role in the recommendation and prescription of any product candidates for which Tempest obtains marketing approval. Tempest's future arrangements with providers, third-party payors and customers will subject Tempest to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which Tempest markets, sells and distributes any product candidates for which Tempest obtains marketing approval.

Restrictions under applicable U.S. federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, a criminal law that prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of the federal Anti-Kickback Statute or specific intent to violate it in order to have committed a violation. Violations of the federal Anti-Kickback Statute can result in significant civil monetary penalties and criminal fines, as well as imprisonment and exclusion from participation in federal health care programs;
- the federal civil False Claims Act, imposes significant civil penalties and treble damages, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, the government may assert that a claim including items or services resulting from a violation of the U.S. federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act;
- the federal Criminal Statute on False Statements Relating to Health Care Matters makes it a crime to knowingly and willfully falsify, conceal, or cover up a material fact, make any materially false, fictitious, or fraudulent statements or representations, or make or use any materially false writing or document knowing the same to contain any materially false, fictitious, or fraudulent statement or entry in connection with the delivery of or payment for healthcare benefits, items, or services;
- the Federal Civil Monetary Penalties Law authorizes the imposition of substantial civil monetary penalties against an entity that engages in activities including, among others (1) knowingly presenting, or causing to be presented, a claim for services not provided as claimed or that is otherwise false or fraudulent in any way; (2) arranging for or contracting with an individual or entity that is excluded from participation in federal health care programs to provide items or services reimbursable by a federal health care program; (3) violations of the federal Anti-Kickback Statute; or (4) failing to report and return a known overpayment;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for, among other things, knowingly and willfully executing or attempting to execute a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters. Similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;
- the federal Physician Payment Sunshine Act requires applicable manufacturers of covered drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program, among others, to track and report payments and other transfers of value provided during the previous year to U.S. licensed physicians, teaching hospitals, and for reports submitted on or after January 1, 2022, physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists, and certified nurse midwives, as well as certain ownership and investment interests held by physicians and their immediate family;
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; and
- some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government and may require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures.

Efforts to ensure that Tempest's business arrangements with third parties will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that Tempest's business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If Tempest's operations are found to be in violation of any of these laws or any other governmental regulations that may apply to Tempest, Tempest may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion from government-funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and future earnings, and the curtailment or restructuring of Tempest's operations. If any of the physicians or other healthcare providers or entities with whom Tempest expects to do business is found to be not in compliance with applicable laws, it may be costly to Tempest in terms of money, time and resources, and Tempest may be subject to criminal, civil or administrative sanctions, including exclusion from government-funded healthcare programs.

Risks Related to Tempest's Intellectual Property

Tempest's success depends in part on its ability to obtain, maintain and protect its intellectual property. It is difficult and costly to protect Tempest's proprietary rights and technology, and Tempest may not be able to ensure their protection.

Tempest's commercial success will depend in large part on obtaining and maintaining patent, trademark, trade secret and other intellectual property protection of Tempest's proprietary technologies and product candidates, which include TPST-1495, TPST-1120 and the other product candidates Tempest has in development, their respective components, formulations, combination therapies, methods used to manufacture them and methods of treatment, as well as successfully defending Tempest's patents and other intellectual property rights against third-party challenges. Tempest's ability to stop unauthorized third parties from making, using, selling, offering to sell, importing or otherwise commercializing Tempest's product candidates is dependent upon the extent to which Tempest has rights under valid and enforceable patents or trade secrets that cover these activities. If Tempest is unable to secure and maintain patent protection for any product or technology Tempest develops, or if the scope of the patent protection secured is not sufficiently broad, Tempest's competitors could develop and commercialize products and technology similar or identical to Tempest's, and Tempest's ability to commercialize any product candidates Tempest may develop may be adversely affected.

The patenting process is expensive and time-consuming, and Tempest may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. In addition, Tempest may not pursue or obtain patent protection in all relevant markets. It is also possible that Tempest will fail to identify patentable aspects of Tempest's research and development activities before it is too late to obtain patent protection. Moreover, in some circumstances, Tempest may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that Tempest licenses from or licenses to third parties and may be reliant on Tempest's licensors or licensees to do so. Tempest's pending and future patent applications may not result in issued patents. Even if patent applications Tempest licenses or owns currently or in the future issue as patents, they may not issue in a form that will provide Tempest with any meaningful protection, prevent competitors or other third parties from competing with Tempest, or otherwise provide Tempest with any competitive advantage. Any patents that Tempest holds or in-licenses may be challenged, narrowed, circumvented or invalidated by third parties. Consequently, Tempest does not know whether any of Tempest's platform advances and product candidates will be protectable or remain protected by valid and enforceable patents. In addition, Tempest's existing patents and any future patents Tempest obtains may not be sufficiently broad to prevent others from using Tempest's technology or from developing competing products and technologies.

In the future, Tempest may depend on intellectual property licensed from third parties, and its licensors may not always act in Tempest's best interest. If Tempest fails to comply with its obligations under its intellectual property licenses, if the licenses are terminated, or if disputes regarding these licenses arise, Tempest could lose significant rights that may be important to its business.

Although it is currently not the case, Tempest may in the future depend on patents, know-how and proprietary technology licensed from third parties. Tempest's licenses to such patents, know-how and proprietary technology may not provide exclusive rights in all relevant fields of use and in all territories in which Tempest may wish to develop or commercialize Tempest's products in the future. The agreements under which Tempest licenses patents, know-how and proprietary technology from others may be complex, and certain provisions in such agreements may be susceptible to multiple interpretations.

Tempest may need to obtain licenses from third parties to advance Tempest's research or allow commercialization of product candidates Tempest may develop. It is possible that Tempest may be unable to obtain any licenses at a reasonable cost or on reasonable terms, if at all. In either event, Tempest may be required to expend significant time and resources to redesign Tempest's technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If Tempest is unable to do so, Tempest may be unable to develop or commercialize the affected technology or product candidates.

If Tempest's future licensors fail to adequately protect Tempest's licensed intellectual property, Tempest's ability to commercialize product candidates could suffer. Tempest may not have complete control over the maintenance, prosecution and litigation of Tempest's future in-licensed patents and patent applications. For example, Tempest cannot be certain that activities such as the maintenance and prosecution by Tempest's future licensors have been or will be conducted in compliance with applicable laws and regulations or will result in valid and enforceable patents and other intellectual property rights. It is possible that future Tempest's licensors' infringement proceedings or defense activities may be less vigorous than had Tempest conducted them itself or may not be conducted in accordance with Tempest's best interests.

In addition, the resolution of any contract interpretation disagreement that may arise could narrow what Tempest might believe to be the scope of Tempest's rights to the relevant patents, know-how and proprietary technology, or increase what Tempest believes to be Tempest's financial or other obligations under the relevant agreement. Disputes that may arise between Tempest and Tempest's future licensors regarding intellectual property subject to a license agreement could include disputes regarding:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- whether and the extent to which Tempest's technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- Tempest's right to sublicense patent and other rights to third parties under collaborative development relationships;
- Tempest's diligence obligations with respect to the use of the licensed technology in relation to Tempest's development and commercialization of Tempest's product candidates and what activities satisfy those diligence obligations;
- royalty, milestone or other payment obligations that may result from the advancement or commercial sale of any of Tempest's product candidates; and
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by Tempest's licensors and Tempest.

If disputes over intellectual property that Tempest licenses in the future prevent or impair Tempest's ability to maintain Tempest's licensing arrangements on acceptable terms, Tempest may be unable to successfully develop and commercialize the affected technology or product candidates.

Tempest's owned and in-licensed patents and patent applications may not provide sufficient protection of Tempest's product candidates or result in any competitive advantage.

The patent position of biopharmaceutical companies generally is highly uncertain, involves complex legal and factual questions, and has been the subject of much litigation in recent years. As a result, the issuance, scope, validity, enforceability and commercial value of Tempest's patent rights is highly uncertain. Tempest's pending and future patent applications and those of its licensors may not result in patents being issued which protect its product candidates or which effectively prevent others from commercializing competitive product candidates.

The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that Tempest owns or, in the future, in-license may fail to result in issued patents with claims that cover Tempest's product candidates or uses thereof in the United States or in other foreign countries. For example, while Tempest's patent applications are pending, Tempest may be subject to a third party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in interference or derivation proceedings, or equivalent proceedings in foreign jurisdictions. Even if patents do successfully issue, third parties may challenge their inventorship, validity, enforceability or scope, including through opposition, revocation, reexamination, post-grant and *inter partes* review proceedings. An adverse determination in any such submission, proceeding or litigation may result in loss of patent rights, loss of exclusivity, or in patent claims being narrowed, invalidated or held unenforceable, which could limit Tempest's ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of Tempest's technology and product candidates. Furthermore, even if they are unchallenged, Tempest's patents and patent applications may not adequately protect Tempest's intellectual property or prevent others from designing around Tempest's claims. Moreover, some of Tempest's owned and in-licensed patents and patent applications may be co-owned with third parties. If Tempest is unable to obtain an exclusive license to any such third-party co-owners' interest in such patents or patent applications, such co-owners may be able to license their rights to other third parties, including Tempest's competitors, and Tempest's competitors could market competing products and technology. In addition, Tempest may need the cooperation of any such co-owners of Tempest's patents in order to enforce such patents against third parties, and such cooperation may not be provided to Tempest. If the breadth or strength of protection provided by the patent applications Tempest holds with respect to Tempest's product candidates is threatened, it could dissuade companies from collaborating with Tempest to develop, and threaten Tempest's ability to commercialize, Tempest's product candidates. Further, if Tempest encounters delays in development, testing, and regulatory review of new product candidates, the period of time during which Tempest could market Tempest's product candidates under patent protection would be reduced or eliminated.

Since patent applications in the United States and other countries are confidential for a period of time after filing or until issuance, at any moment in time, Tempest cannot be certain that it was in the past or will be in the future the first to file any patent application related to Tempest's product candidates. In addition, some patent applications in the United States may be maintained in secrecy until the patents are issued. As a result, there may be prior art of which Tempest is not aware that may affect the validity or enforceability of a patent claim, and Tempest may be subject to priority disputes. Tempest may be required to disclaim part or all of the term of certain patents or all of the term of certain patent applications. There also may be prior art of which Tempest is aware, but which Tempest does not believe affects the validity or enforceability of a claim, which may, nonetheless, ultimately be found to affect the validity or enforceability of a claim. No assurance can be given that, if challenged, Tempest's patents would be declared by a court, patent office or other governmental authority to be valid or enforceable or that even if found valid and enforceable, a competitor's technology or product would be found by a court to infringe Tempest's patents. Tempest may analyze patents or patent applications of Tempest's competitors that Tempest believes are relevant to Tempest's activities, and consider that Tempest is free to operate in relation to Tempest's product candidates, but Tempest's competitors may achieve issued claims, including in patents Tempest considers to be unrelated, that block Tempest's efforts or potentially result in Tempest's product candidates or Tempest's activities infringing such claims. It is possible that Tempest's competitors may have filed, and may in the future file, patent applications covering Tempest's products or technology similar to Tempest's. Those patent applications may have priority over Tempest's owned and in-licensed patent applications or patents, which could require Tempest to obtain rights to issued patents covering such technologies. The possibility also exists that others will develop products that have the same effect as Tempest's product candidates on an independent basis that do not infringe Tempest's patents or other intellectual property rights, or will design around the claims of patents that Tempest has had issued that cover Tempest's product candidates or their use. Likewise, Tempest's currently owned patents and patent applications, if issued as patents, directed to Tempest's proprietary technologies and Tempest's product candidates are expected to expire from 2033 through 2041, without taking into account any possible patent term adjustments or extensions. Tempest's earliest patents may expire before, or soon after, Tempest's first product achieves marketing approval in the United States or foreign jurisdictions. Additionally, Tempest cannot be assured that the USPTO or relevant foreign patent offices will grant any of the pending patent applications Tempest owns or in-licenses currently or in the future. Upon the expiration of Tempest's current patents, Tempest may lose the right to exclude others from practicing these inventions. The expiration of these patents could also have a similar material adverse effect on Tempest's business, financial condition, results of operations and prospects.

The degree of future protection for Tempest's proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect Tempest's rights or permit Tempest to gain or keep Tempest's competitive advantage. For example:

- others may be able to make or use compounds that are similar to the active compositions of Tempest's product candidates but that are not covered by the claims of Tempest's patents;
- the APIs in Tempest's current product candidates will eventually become commercially available in generic drug products, and no patent protection may be available with regard to formulation or method of use;

- Tempest or Tempest's future licensors, as the case may be, may fail to meet its or Tempest's obligations to the U.S. government regarding any patents and patent applications funded by U.S. government grants, leading to the loss or unenforceability of patent rights;
- Tempest or Tempest's future licensors, as the case may be, might not have been the first to file patent applications for certain inventions;
- others may independently develop similar or alternative technologies or duplicate any of Tempest's technologies;
- it is possible that Tempest's pending patent applications will not result in issued patents;
- it is possible that there are prior public disclosures that could invalidate Tempest's owned or in-licensed patents, as the case may be, or parts of Tempest's owned or in-licensed patents;
- it is possible that others may circumvent Tempest's owned or in-licensed patents;
- it is possible that there are unpublished applications or patent applications maintained in secrecy that may later issue with claims covering Tempest's product candidates or technology similar to Tempest's;
- the laws of foreign countries may not protect Tempest's or Tempest's future licensors', as the case may be, proprietary rights to the same extent as the laws of the United States;
- the claims of Tempest's owned or in-licensed issued patents or patent applications, if and when issued, may not adequately cover Tempest's product candidates;
- Tempest's owned or in-licensed issued patents may not provide Tempest with any competitive advantages, may be narrowed in scope, or be held invalid or unenforceable as a result of legal challenges by third parties;
- the inventors of Tempest's owned or in-licensed patents or patent applications may become involved with competitors, develop products or processes that design around Tempest's patents, or become hostile to Tempest or the patents or patent applications on which they are named as inventors;
- it is possible that Tempest's owned or in-licensed patents or patent applications may omit individual(s) that should be listed as inventor(s) or include individual(s) that should not be listed as inventor(s), which may cause these patents or patents issuing from these patent applications to be held invalid or unenforcbeable or such omitted individuals may grant licenses to third parties;
- Tempest has engaged in scientific collaborations in the past and will continue to do so in the future and Tempest's collaborators may develop adjacent or competing products that are outside the scope of Tempest's patents;
- Tempest may not develop additional proprietary technologies for which Tempest can obtain patent protection;
- it is possible that product candidates or diagnostic tests Tempest develops may be covered by third parties' patents or other exclusive rights; or
- the patents of others may have an adverse effect on Tempest's business.

Any of the foregoing could have a material adverse effect on Tempest's business, financial conditions, results of operations and prospects.

Tempest's strategy of obtaining rights to key technologies through in-licenses may not be successful.

The future growth of Tempest's business may depend in part on Tempest's ability to in-license or otherwise acquire the rights to additional product candidates and technologies. Tempest cannot assure you that Tempest will be able to in-license or acquire the rights to any product candidates or technologies from third parties on acceptable terms or at all.

For example, Tempest's agreements with certain of its third-party research partners provide that improvements developed in the course of its relationship may be owned solely by either Tempest or its third-party research partner, or jointly between Tempest and the third party. If Tempest determines that exclusive rights to such improvements owned solely by a research partner or other third party with whom Tempest collaborates are necessary to commercialize Tempest's drug candidates or maintain Tempest's competitive advantage, Tempest may need to obtain an exclusive license from such third party in order to use the improvements and continue developing, manufacturing or marketing Tempest's drug candidates. Tempest may not be able to obtain such a license on an exclusive basis, on commercially reasonable terms, or at all, which could prevent Tempest from commercializing its drug candidates or allow Tempest's competitors or others the opportunity to access technology that is important to Tempest's business. Tempest also may need the cooperation of any co-owners of Tempest's intellectual property in order to enforce such intellectual property against third parties, and such cooperation may not be provided to Tempest.

In addition, the in-licensing and acquisition of these technologies is a highly competitive area, and a number of more established companies are also pursuing strategies to license or acquire product candidates or technologies that Tempest may consider attractive. These established companies may have a competitive advantage over Tempest due to their size, cash resources and greater clinical development and commercialization capabilities. In addition, companies that perceive Tempest to be a competitor may be unwilling to license rights to Tempest. Furthermore, Tempest may be unable to identify suitable product candidates or technologies within Tempest's area of focus. If Tempest is unable to successfully obtain rights to suitable product candidates or technologies, Tempest's business and prospects could be materially and adversely affected.

If Tempest is unable to protect the confidentiality of its trade secrets, Tempest's business and competitive position would be harmed.

In addition to patent protection, Tempest relies upon know-how and trade secret protection, as well as non-disclosure agreements and invention assignment agreements with Tempest's employees, consultants and third-parties, to protect Tempest's confidential and proprietary information, especially where Tempest does not believe patent protection is appropriate or obtainable.

It is Tempest's policy to require Tempest's employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with Tempest. These agreements provide that all confidential information concerning Tempest's business or financial affairs developed or made known to the individual or entity during the course of the party's relationship with Tempest is to be kept confidential and not disclosed to third parties, except in certain specified circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and that are related to Tempest's current or planned business or research and development or made during normal working hours, on Tempest's premises or using Tempest's equipment or proprietary information (or as otherwise permitted by applicable law), are Tempest's exclusive property. In the case of consultants and other third parties, the agreements provide that all inventions conceived in connection with the services provided are Tempest's exclusive property. However, Tempest cannot guarantee that Tempest has entered into such agreements with each party that may have or have had access to Tempest's trade secrets or proprietary technology and processes. Tempest has also adopted policies and conducts training that provides guidance on Tempest's expectations, and Tempest's advice for best practices, in protecting its trade secrets. Despite these efforts, any of these parties may breach the agreements and disclose Tempest's proprietary information, including its trade secrets, and Tempest may not be able to obtain adequate remedies for such breaches.

In addition to contractual measures, Tempests tries to protect the confidential nature of Tempest's proprietary information through other appropriate precautions, such as physical and technological security measures. However, trade secrets and know-how can be difficult to protect. These measures may not, for example, in the case of misappropriation of a trade secret by an employee or third party with authorized access, provide adequate protection for Tempest's proprietary information. Tempest's security measures may not prevent an employee or consultant from misappropriating Tempest's trade secrets and providing them to a competitor, and any recourse Tempest might take against this type of misconduct may not provide an adequate remedy to protect Tempest's interests fully. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret can be difficult, expensive, and time-consuming, and the outcome is unpredictable. In addition, trade secrets may be independently developed by others in a manner that could prevent Tempest from receiving legal recourse. If any of Tempest's confidential or proprietary information, such as its trade secrets, were to be disclosed or misappropriated, such as through a data breach, or if any of that information was independently developed by a competitor, Tempest's competitive position could be harmed. Additionally, certain trade secret and proprietary information may be required to be disclosed in submissions to regulatory authorities. If such authorities do not maintain the confidential basis of such information or disclose it as part of the basis of regulatory approval, Tempest's competitive position could be adversely affected.

In addition, courts outside the United States are sometimes less willing to protect trade secrets. If Tempest chooses to go to court to stop a third party from using any of Tempest's trade secrets, Tempest may incur substantial costs. Even if Tempest is successful, these types of lawsuits may result in substantial cost and require significant time from our scientists and management. Although Tempest takes steps to protect Tempest's proprietary information and trade secrets, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to Tempest's trade secrets or disclose Tempest's technology, through legal or illegal means. As a result, Tempest may not be able to meaningfully protect its trade secrets. Any of the foregoing could have a material adverse effect on Tempest's business, financial condition, results of operations and prospects.

Third-party claims of intellectual property infringement may prevent, delay or otherwise interfere with Tempest's product discovery and development efforts.

Tempest's commercial success depends in part on Tempest's ability to develop, manufacture, market and sell Tempest's product candidates and use Tempest's proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property or other proprietary rights of third parties. There is a substantial amount of litigation involving patents and other intellectual property rights in the biotechnology and pharmaceutical industries, as well as administrative proceedings for challenging patents, including interference, derivation, inter partes review, post grant review, and reexamination proceedings before the USPTO or oppositions and other comparable proceedings in foreign jurisdictions. Tempest may be exposed to, or threatened with, future litigation by third parties having patent or other intellectual property rights alleging that Tempest's product candidates and/or proprietary technologies infringe, misappropriate or otherwise violate their intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications that are owned by third parties exist in the fields in which Tempest is developing Tempest's product candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that Tempest's product candidates may give rise to claims of infringement of the patent rights of others. Moreover, it is not always clear to industry participants, including Tempest, which patents cover various types of drugs, products or their methods of use or manufacture. Thus, because of the large number of patents issued and patent applications filed in Tempest's field, third parties may allege they have patent rights encompassing Tempest's product candidates, technologies or methods.

If a third-party claims that Tempest infringes, misappropriates or otherwise violates its intellectual property rights, Tempest may face a number of issues, including, but not limited to:

- infringement and other intellectual property claims that, regardless of merit, may be expensive and time-consuming to litigate and may divert Tempest's management's attention from its core business;
- substantial damages for infringement, which Tempest may have to pay if a court decides that the product candidate or technology at issue infringes on or violates the third party's rights, and, if the court finds that the infringement was willful, Tempest could be ordered to pay treble damages plus the patent owner's attorneys' fees;
- a court prohibiting Tempest from developing, manufacturing, marketing or selling Tempest's product candidates, or from using Tempest's proprietary technologies, unless the third-party licenses its product rights or proprietary technology to Tempest, which it is not required to do, on commercially reasonable terms or at all;
- if a license is available from a third party, Tempest may have to pay substantial royalties, upfront fees and other amounts, and/or grant cross-licenses to intellectual property rights for Tempest's product candidates;
- the requirement that Tempest redesign its product candidates or processes so they do not infringe, which may not be possible or may require substantial monetary expenditures and time; and
- there could be public announcements of the results of hearings, motions, or other interim proceedings or developments, and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of Tempest's common stock.

Some of Tempest's competitors may be able to sustain the costs of complex patent litigation more effectively than Tempest can because they have substantially greater resources. In addition, any uncertainties resulting from the initiation and continuation of any litigation could have a material adverse effect on Tempest's ability to raise the funds necessary to continue Tempest's operations or could otherwise have a material adverse effect on Tempest's business, financial condition, results of operations and prospects.

Third parties may assert that Tempest is employing their proprietary technology without authorization, including by enforcing its patents against Tempest by filing a patent infringement lawsuit against Tempest. In this regard, patents issued in the United States by law enjoy a presumption of validity that can be rebutted only with evidence that is "clear and convincing," a heightened standard of proof.

There may be third-party patents of which Tempest is currently unaware with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of Tempest's product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications that may later result in issued patents that Tempest's product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of Tempest's technologies infringes upon these patents.

If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of Tempest's product candidates, or materials used in or formed during the manufacturing process, or any final product itself, the holders of those patents may be able to block Tempest's ability to commercialize Tempest's product candidate unless Tempest obtains a license under the applicable patents, or until those patents were to expire or those patents are finally determined to be invalid or unenforceable. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of Tempest's formulations, processes for manufacture or methods of use, including combination therapy or patient selection methods, the holders of that patent may be able to block Tempest's ability to develop and commercialize the product candidate unless Tempest obtains a license or until such patent expires or is finally determined to be invalid or unenforceable. In either case, a license may not be available on commercially reasonable terms, or at all, particularly if such patent is owned or controlled by one of Tempest's primary competitors. If Tempest is unable to obtain a necessary license to a third-party patent on commercially reasonable terms, or at all, Tempest's ability to commercialize Tempest's product candidates may be impaired or delayed, which could significantly harm Tempest's business. Even if Tempest obtains a license, it may be non-exclusive, thereby giving Tempest's competitors access to the same technologies licensed to Tempest. In addition, if the breadth or strength of protection provided by Tempest's patents and patent applications is threatened, it could dissuade companies from collaborating with Tempest to license, develop or commercialize current or future product candidates.

Parties making claims against Tempest may seek and obtain injunctive or other equitable relief, which could effectively block Tempest's ability to further develop and commercialize Tempest's product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee time and resources from Tempest's business. In the event of a successful claim of infringement against Tempest, Tempest may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign Tempest's infringing products, which may be impossible or require substantial time and monetary expenditure. Tempest cannot predict whether any license of this nature would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, Tempest may need to obtain licenses from third parties to advance Tempest's research or allow commercialization of Tempest's product candidates and Tempest may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, Tempest would be unable to further develop and commercialize Tempest's product candidates, which could significantly harm Tempest's business.

Tempest may be involved in lawsuits to protect or enforce its patents or the patents of its licensors, which could be expensive, time-consuming and unsuccessful and could result in a finding that such patents are unenforceable or invalid.

Competitors may infringe Tempest's patents or the patents of its future licensors. To counter infringement or unauthorized use, Tempest may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one or more of Tempest's patents is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that Tempest's patents do not cover the technology in question.

In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, written description, non-enablement, or obviousness-type double patenting. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. These types of mechanisms include re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). These types of proceedings could result in revocation or amendment to Tempest's patents such that they no longer cover Tempest's product candidates. The outcome for any particular patent following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, Tempest cannot be certain that there is no invalidating prior art, of which Tempest, Tempest's patent counsel and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, or if Tempest is otherwise unable to adequately protect Tempest's rights, Tempest would lose at least part, and perhaps all, of the patent protection on Tempest's product candidates. Defense of these types of claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from Tempest's business.

Conversely, Tempest may choose to challenge the patentability of claims in a third party's U.S. patent by requesting that the USPTO review the patent claims in re-examination, post-grant review, inter partes review, interference proceedings, derivation proceedings, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings), or Tempest may choose to challenge a third party's patent in patent opposition proceedings in the Canadian Intellectual Property Office, or CIPO, the European Patent Office, or EPO, or another foreign patent office. Even if successful, the costs of these opposition proceedings could be substantial, and may consume Tempest's time or other resources. If Tempest fails to obtain a favorable result at the USPTO, CIPO, EPO or other patent office then Tempest may be exposed to litigation by a third party alleging that the patent may be infringed by Tempest's product candidates or proprietary technologies.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of Tempest's confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, that perception could have a substantial adverse effect on the price of Tempest's common stock. Any of the foregoing could have a material adverse effect on Tempest's business financial condition, results of operations and prospects.

Tempest may not be able to protect its intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and Tempest's intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. For example, patents covering methods-of-use are not available in certain foreign countries. Consequently, Tempest may not be able to prevent third parties from practicing Tempest's inventions in all countries outside the United States, or from selling or importing products made using Tempest's inventions in and into the United States or other jurisdictions. Competitors may use Tempest's technologies in jurisdictions where Tempest does not have or has not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where Tempest has patent protection but where enforcement is not as strong as that in the United States. These products may compete with Tempest's product candidates in jurisdictions where Tempest does not have any issued patents and Tempest's patent claims or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biopharmaceutical products, which could make it difficult for Tempest to stop the infringement of Tempest's patents or marketing of competing products against third parties in violation of Tempest's proprietary rights generally. The initiation of proceedings by third parties to challenge the scope or validity of Tempest's patent rights in foreign jurisdictions could result in substantial cost and divert management's efforts and attention from other aspects of Tempest's business. Proceedings to enforce Tempest's patent rights in foreign jurisdictions could result in substantial costs and divert management's efforts and attention from other aspects of Tempest's business, could put Tempest's patents at risk of being invalidated or interpreted narrowly and Tempest's patent applications at risk of not issuing and could provoke third parties to assert claims against Tempest. Tempest may not prevail in any lawsuits that Tempest initiates and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, Tempest's efforts to enforce Tempest's intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that Tempest develops or licenses.

Third parties may assert that Tempest's employees or consultants have wrongfully used or disclosed confidential information or misappropriated trade secrets.

As is common in the biotechnology and pharmaceutical industries, Tempest employs individuals who were previously employed at universities or other biopharmaceutical or pharmaceutical companies, including Tempest's competitors or potential competitors. Although Tempest tries to ensure that Tempest's employees and consultants do not use the proprietary information or know-how of others in their work for Tempest, Tempest may be subject to claims that Tempest's employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third parties. Tempest may then have to pursue litigation to defend against these claims. If Tempest fails in defending any claims of this nature, in addition to paying monetary damages, Tempest may lose valuable intellectual property rights or personnel. Even if Tempest is successful in defending against these types of claims, litigation or other legal proceedings relating to intellectual property claims may cause Tempest to incur significant expenses, and could distract Tempest's technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments, and, if securities analysts or investors perceive these results to be negative, that perception could have a substantial adverse effect on the price of Tempest's common stock. This type of litigation or proceeding could substantially increase Tempest's operating losses and reduce Tempest's resources available for development activities, and Tempest may not have sufficient financial or other resources to adequately conduct this type of litigation or proceedings. For example, some of Tempest's competitors may be able to sustain the costs of this type of litigation or proceedings more effectively than Tempest can because of their substantially greater financial resources. In any case, uncertainties resulting from the initiation and continuation of intellectual property litigation or other intellectual property related proceedings could adversely affect Tempest's ability to compete in the marketplace.

Obtaining and maintaining Tempest's patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and Tempest's patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the USPTO and foreign patent agencies in several stages over the lifetime of the patent. The USPTO and various foreign patent agencies also require compliance with a number of procedural, documentary, fee payment and other provisions during the patent application process and following the issuance of a patent. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable laws and rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Noncompliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. Were a noncompliance event to occur, Tempest's competitors might be able to enter the market, which would have a material adverse effect on Tempest's business financial condition, results of operations and prospects.

Changes in patent law in the United States and in non-U.S. jurisdictions could diminish the value of patents in general, thereby impairing Tempest's ability to protect its product candidates.

As is the case with other biopharmaceutical companies, Tempest's success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain.

Past or future patent reform legislation could increase the uncertainties and costs surrounding the prosecution of Tempest's patent applications and the enforcement or defense of Tempest's issued patents. For example, in March 2013, under the Leahy-Smith America Invents Act, or America Invents Act, the United States moved from a "first to invent" to a "first-to-file" patent system. Under a "first-to-file" system, assuming the other requirements for patentability are met, the first inventor to file a patent application generally will be entitled to a patent on the invention regardless of whether another inventor had made the invention earlier. The America Invents Act includes a number of other significant changes to U.S. patent law, including provisions that affect the way patent applications are prosecuted, redefine prior art and establish a new post-grant review system. The effects of these changes continue to evolve as the USPTO continues to promulgate new regulations and procedures in connection with the America Invents Act. In addition, the courts have yet to address many of these provisions and the applicability of the act and new regulations on the specific patents discussed in this filing have not been determined and would need to be reviewed. Moreover, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of Tempest's patent applications and the enforcement or defense of Tempest's issued patents.

Additionally, recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to Tempest's ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the U.S. Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken Tempest's ability to obtain new patents or to enforce Tempest's existing patents and patents that Tempest might obtain or license in the future. For example, in the case, *Assoc. for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to DNA molecules are not patent-eligible.

Similarly, other cases by the U.S. Supreme Court have held that certain methods of treatment or diagnosis are not patent-eligible. U.S. law regarding patent-eligibility continues to evolve. While Tempest does not believe that any of Tempest's patents will be found invalid based on these changes to US patent law, Tempest cannot predict how future decisions by the courts, the U.S. Congress or the USPTO may impact the value of Tempest's patents and patent applications. Any similar adverse changes in the patent laws of other jurisdictions could also have a material adverse effect on Tempest's business, financial condition, results of operations and prospects.

Patent terms may be inadequate to protect Tempest's competitive position on its product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering Tempest's product candidates are obtained, once the patent life has expired, Tempest may be open to competition from competitive products, including generics. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting Tempest's product candidates might expire before or shortly after Tempest or Tempest's partners commercialize those candidates. As a result, Tempest's owned and licensed patent portfolio may not provide Tempest with sufficient rights to exclude others from commercializing products similar or identical to Tempest's.

If Tempest does not obtain patent term extension for any product candidates it may develop, Tempest's business may be materially harmed.

Depending upon the timing, duration and specifics of any FDA marketing approval of any product candidates Tempest may develop, one or more of Tempest's U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent extension term of up to five years as compensation for patent term lost during clinical trials and the FDA regulatory review process. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, only one patent per product may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. U.S. and ex-U.S. law concerning patent term extensions and foreign equivalents continue to evolve. Even if Tempest were to seek a patent term extension, it may not be granted because of, for example, the failure to exercise due diligence during the testing phase or regulatory review process, the failure to apply within applicable deadlines, the failure to apply prior to expiration of relevant patents, or any other failure to satisfy applicable requirements. Moreover, the applicable time period of extension or the scope of patent protection afforded could be less than Tempest requests. If Tempest is unable to obtain patent term extension or term of any such extension is less than it requests, Tempest's competitors may obtain approval of competing products following Tempest's patent expiration sooner than expected, and Tempest's business, financial condition, results of operations and prospects could be materially harmed.

Intellectual property discovered through government funded programs may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit Tempest's exclusive rights and limit its ability to contract with non-U.S. manufacturers.

Although Tempest does not currently own issued patents or pending patent applications that have been generated through the use of U.S. government funding, Tempest may acquire or license in the future intellectual property rights that have been generated through the use of U.S. government funding or grants. Pursuant to the Bayh-Dole Act of 1980, the U.S. government has certain rights in inventions developed with government funding. These U.S. government rights include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (1) adequate steps have not been taken to commercialize the invention; (2) government action is necessary to meet public health or safety needs; or (3) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). If the U.S. government exercised its march-in rights in Tempest's future intellectual property rights that are generated through the use of U.S. government funding or grants, Tempest could be forced to license or sublicense intellectual property developed by Tempest or that Tempest licenses on terms unfavorable to Tempest, and there can be no assurance that Tempest would receive compensation from the U.S. government for the exercise of such rights. The U.S. government also has the right to take title to these inventions if the grant recipient fails to disclose the invention to the government or fails to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require Tempest to expend substantial resources. In addition, the U.S. government requires that any products embodying any of these inventions or produced through the use of any of these inventions be manufactured substantially in the United States. This preference for U.S. industry may be waived by the federal agency that provided the funding if the owner or assignee of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. industry may limit Tempest's ability to contract with non-U.S. product manufacturers for products covered by such intellectual property.

Risks Related to Employee Matters, Managing Growth and Other Risks Related to Tempest's Business

Tempest expects to expand its development and regulatory capabilities, and as a result, Tempest may encounter difficulties in managing its growth, which could disrupt Tempest's operations.

Tempest expects to experience significant growth in the number of Tempest's employees and the scope of Tempest's operations, particularly in the areas of product candidate development, growing Tempest's capability to conduct clinical trials, and, if approved, through commercialization of Tempest's product candidates. To manage its anticipated future growth, Tempest must continue to implement and improve its managerial, operational and financial systems, expand its facilities and continue to recruit and train additional qualified personnel, or contract with third parties to provide these capabilities for Tempest. Due to Tempest's limited financial resources and the limited experience of Tempest's management team in managing a company with such anticipated growth, Tempest may not be able to effectively manage the expansion of Tempest's operations or recruit and train additional qualified personnel. The expansion of Tempest's operations may lead to significant costs and may divert Tempest's management and business development resources. Any inability to manage growth could delay the execution of Tempest's business plans or disrupt Tempest's operations.

Tempest must attract and retain highly skilled employees to succeed.

To succeed, Tempest must recruit, retain, manage and motivate qualified clinical, scientific, technical and management personnel, and Tempest faces significant competition for experienced personnel. If Tempest does not succeed in attracting and retaining qualified personnel, particularly at the management level, it could adversely affect Tempest's ability to execute its business plan, harm Tempest's results of operations and increase Tempest's capabilities to successfully commercialize its product candidates. In particular, Tempest believes that its future success is highly dependent upon the contributions of its senior management, particularly its Chief Executive Officer, Stephen Brady, its President, Tom Dubensky and its Chief Medical Officer, Sam Whiting. The loss of services of Messrs. Dubensky or Brady or Whiting, or any of Tempest's other senior management, could delay or prevent the successful development of Tempest's product pipeline, completion of Tempest's planned clinical trials or the commercialization of Tempest's product candidates, if approved. The competition for qualified personnel in the biotechnology field is intense and as a result, Tempest may be unable to continue to attract and retain qualified personnel necessary for the development of Tempest's business or to recruit suitable replacement personnel.

Many of the other biotechnology companies that Tempest competes against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than Tempest does. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high-quality candidates than what Tempest has to offer. If Tempest is unable to continue to attract and retain high-quality personnel, the rate and success at which Tempest can discover and develop product candidates and Tempest's business will be limited.

Future acquisitions or strategic alliances could disrupt Tempest's business and harm Tempest's financial condition and results of operations.

Tempest may acquire additional businesses or drugs, form strategic alliances or create joint ventures with third parties that Tempest believes will complement or augment Tempest's existing business. If Tempest acquires businesses with promising markets or technologies, Tempest may not be able to realize the benefit of acquiring such businesses if Tempest is unable to successfully integrate them with Tempest's existing operations and company culture. Tempest may encounter numerous difficulties in developing, manufacturing and marketing any new drugs resulting from a strategic alliance or acquisition that delay or prevent Tempest from realizing their expected benefits or enhancing Tempest's business. Tempest cannot assure you that, following any such acquisition, Tempest will achieve the expected synergies to justify the transaction. The risks Tempest faces in connection with acquisitions, include:

- diversion of management time and focus from operating Tempest's business to addressing acquisition integration challenges;
- coordination of research and development efforts;
- retention of key employees from the acquired company;
- changes in relationships with strategic partners as a result of product acquisitions or strategic positioning resulting from the acquisition;
- cultural challenges associated with integrating employees from the acquired company into Tempest's organization;
- the need to implement or improve controls, procedures and policies at a business that prior to the acquisition may have lacked sufficiently effective controls, procedures and policies;
- liability for activities of the acquired company before the acquisition, including intellectual property infringement claims, violation of laws, commercial disputes, tax liabilities and other known liabilities;
- unanticipated write-offs or charges; and
- litigation or other claims in connection with the acquired company, including claims from terminated employees, customers, former stockholders or other third parties.

Tempest's failure to address these risks or other problems encountered in connection with its past or future acquisitions or strategic alliances could cause Tempest to fail to realize the anticipated benefits of these transactions, cause Tempest to incur unanticipated liabilities and harm the business generally. There is also a risk that future acquisitions will result in the incurrence of debt, contingent liabilities, amortization expenses or incremental operating expenses, any of which could harm Tempest's financial condition or results of operations.

If Tempest fails to comply with environmental, health, and safety laws and regulations, Tempest could become subject to fines or penalties or incur costs that could harm Tempest's business.

Tempest is subject to numerous environmental, health, and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Tempest's operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Tempest's operations also may produce hazardous waste products. Tempest generally contracts with third parties for the disposal of these materials and wastes. Tempest will not be able to eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from any use by Tempest of hazardous materials, Tempest could be held liable for any resulting damages, and any liability could exceed Tempest's resources. Tempest also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although Tempest maintains workers' compensation insurance to cover Tempest for costs and expenses Tempest may incur due to injuries to Tempest's employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities.

In addition, Tempest may incur substantial costs in order to comply with current or future environmental, health, and safety laws and regulations. These current or future laws and regulations may impair Tempest's research, development or production efforts. Tempest's failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Unfavorable global economic conditions could adversely affect Tempest's business, financial condition, stock price and results of operations.

Tempest's results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. For example, a global economic downturn that could result from the COVID-19 pandemic could cause extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn could result in a variety of risks to Tempest's business, including, weakened demand for Tempest's product candidates and Tempest's ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain Tempest's suppliers, possibly resulting in supply disruption, or cause Tempest's customers to delay making payments for Tempest's services. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on Tempest's growth strategy, financial performance and stock price and could require Tempest to delay or abandon clinical development plans. In addition, there is a risk that one or more of Tempest's current service providers, manufacturers and other partners may not survive such difficult economic times, which could directly affect Tempest's ability to attain Tempest's operating goals on schedule and on budget. Any of the foregoing could harm Tempest's business and Tempest cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact Tempest's business. Furthermore, our stock price may decline due in part to the volatility of the stock market and any general economic downturn.

Tempest or the third parties upon whom Tempest depends may be adversely affected by natural disasters and other calamities, including pandemics, such as the global outbreak of COVID-19, and Tempest's business continuity and disaster recovery plans may not adequately protect Tempest from a serious disaster.

Natural disasters could severely disrupt Tempest's operations and have a material adverse effect on Tempest's business, results of operations, financial condition and prospects. If a natural disaster, fire, hurricane, power outage or other event occurred that prevented Tempest from using all or a significant portion of Tempest's headquarters, that damaged critical infrastructure, such as Tempest's suppliers' manufacturing facilities, or that otherwise disrupted operations, such as data storage, it may be difficult or, in certain cases, impossible for Tempest to continue Tempest's business for a substantial period of time.

Occurrences of epidemics or pandemics, depending on their scale, may cause different degrees of damage to the national and local economies within Tempest's geographic focus. Global economic conditions may be disrupted by widespread outbreaks of infectious or contagious diseases, and such disruption may adversely affect clinical development plans. For example, the COVID-19 pandemic could have an adverse effect on the coordination of research and development, Tempest's capital raising efforts, and the financial condition of Tempest's business, as well as the ability of Tempest to retain key personnel and continue to expand product candidate development and conduct clinical trials. In addition, the impact of COVID-19 is likely to continue to cause substantial changes in consumer behavior and has caused restrictions on business and individual activities, which are likely to lead to reduced economic activity. Extraordinary actions taken by international, federal, state and local public health and governmental authorities to contain and combat the outbreak and spread of COVID-19 in regions throughout the world, including travel bans, quarantines, "stay-at-home" orders and similar mandates for many individuals and businesses to substantially restrict daily activities could have an adverse effect on Tempest's financial condition and ability to raise financing.

The disaster recovery and business continuity plans Tempest has in place may prove inadequate in the event of a serious disaster or similar event. Tempest may incur substantial expenses as a result of the limited nature of Tempest's disaster recovery and business continuity plans, which could have a material adverse effect on Tempest's business. As a result of the COVID-19 pandemic, Tempest may experience reduction in research and development, clinical testing, regulatory compliance activities, and manufacturing activities, and is unable at this time to estimate the extent of the effect of COVID-19 on its business. The extent and duration of the economic slowdown attributable to COVID-19 remains uncertain at this time. A continued significant economic slowdown could have a substantial adverse effect on Tempest's financial condition, liquidity, and results of operations. If these conditions persist for an extended term, it could have a material adverse effect on Tempest's future revenue and sales.

Tempest's internal computer and information systems, or those used by its CROs, CMOs or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of Tempest's development programs.

Despite the implementation of appropriate security measures, Tempest's internal computer and information systems and those of Tempest's current and any future CROs, CMOs and other contractors or consultants may become vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If such an event were to occur and cause interruptions in Tempest's operations, it could result in a material disruption of Tempest's development programs and Tempest's business operations, whether due to a loss of Tempest's trade secrets or other proprietary information or other similar disruptions. For example, the loss of data from completed or future preclinical studies or clinical trials could result in significant delays in Tempest's regulatory approval efforts and significantly increase Tempest's costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, Tempest's data or applications, or inappropriate disclosure of confidential or proprietary information, Tempest could incur liability, Tempest's competitive position could be harmed and the further development and commercialization of Tempest's product candidates could be significantly delayed. Tempest's internal information technology systems and infrastructure are also vulnerable to damage from natural disasters, terrorism, war, telecommunication and electrical failures. System failures or outages, including any potential disruptions due to significantly increased global demand on certain cloud-based systems during the COVID-19 pandemic, could compromise Tempest's ability to perform its day-to-day operations, which could harm its ability to conduct business or delay its financial reporting. Such failures could materially adversely affect Tempest's operating results and financial condition.

Tempest is subject to a variety of privacy and data security laws, and Tempest's failure to comply with them could harm Tempest's business.

Tempest maintains a large quantity of sensitive information, including confidential business and patient health information in connection with Tempest's preclinical and clinical studies, and is subject to laws and regulations governing the privacy and security of such information. In the United States, there are numerous federal and state privacy and data security laws and regulations governing the collection, use, disclosure and protection of personal information, including health information privacy laws, security breach notification laws, and consumer protection laws. Each of these laws is subject to varying interpretations and constantly evolving. In addition, Tempest may obtain health information from third parties (including research institutions from which it obtains clinical trial data) that are subject to privacy and security requirements under HIPAA. Depending on the facts and circumstances, Tempest could be subject to criminal penalties if it knowingly obtains, uses or discloses individually identifiable health information maintained by a HIPAA covered entity in a manner that is not authorized or permitted by HIPAA.

Certain states have also adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. For example, California enacted the California Consumer Privacy Act, or the CCPA, which took effect on January 1, 2020. The CCPA gives California residents expanded rights to access and delete their personal information, opt out of certain personal information sharing, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA may increase Tempest's compliance costs and potential liability. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the United States, which could increase Tempest's potential liability and adversely affect Tempest's business.

In Canada, the Personal Information Protection and Electronic Documents Act, or PIPEDA, and similar provincial laws may impose obligations with respect to processing personal information, including health-related information. PIPEDA requires companies to obtain an individual's consent when collecting, using or disclosing that individual's personal information. Individuals have the right to access and challenge the accuracy of their personal information held by an organization, and personal information may only be used for the purposes for which it was collected. If an organization intends to use personal information for another purpose, it must again obtain that individual's consent. Failure to comply with PIPEDA could result in significant fines and penalties.

In May 2018, the General Data Protection Regulation, or the GDPR, took effect in the European Economic Area, the EEA. The GDPR governs the collection, use, disclosure, transfer or other processing of personal data of natural persons. Among other things, the GDPR imposes strict obligations on the ability to process health-related and other personal data of data subjects in the EEA, including in relation to use, collection, analysis and transfer (including cross-border transfer) of such personal data. The GDPR includes requirements relating to the consent of the individuals to whom the personal data relates, including detailed notices for clinical trial subjects and investigators. The GDPR also includes certain requirements regarding the security of personal data and notification of data processing obligations or security incidents to appropriate data protection authorities or data subjects as well as requirements for establishing a lawful basis on which personal data can be processed. In addition, the GDPR increases the scrutiny of transfers of personal data from clinical trial sites located in the EEA to the United States and other jurisdictions that the European Commission does not recognize as having "adequate" data protection laws, and imposes substantial fines for breaches and violations (up to the greater of €20 million or 4% of Tempest's annual worldwide gross revenue). Further, recent legal developments in Europe have created complexity and compliance uncertainty regarding certain transfers of information from the EEA to the United States. For example, on June 16, 2020, the Court of Justice of the European Union, or the CJEU, declared the EU-U.S. Privacy Shield framework, or the Privacy Shield, to be invalid. As a result, Privacy Shield is no longer a valid mechanism for transferring personal data from the EEA to the United States. Moreover, it is uncertain whether the standard contractual clauses will also be invalidated by the European courts or legislature, which seems possible given the rationale behind the CJEU's concerns about U.S. law and practice on government surveillance. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies and obtain compensation for damages resulting from violations of the GDPR.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and Tempest may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. If Tempest fails to comply with any such laws or regulations, Tempest may face significant fines and penalties that could adversely affect Tempest's business, financial condition and results of operations.

Tempest may be unable to adequately protect its information systems from cyberattacks, which could result in the disclosure of confidential information, damage Tempest's reputation, and subject Tempest to significant financial and legal exposure.

Cyberattacks are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. Cyberattacks could include wrongful conduct by hostile foreign governments, industrial espionage, wire fraud and other forms of cyber fraud, the deployment of harmful malware, denial-of-service, social engineering fraud or other means to threaten data confidentiality, integrity and availability. A successful cyberattack could cause serious negative consequences for Tempest, including, without limitation, the disruption of operations, the misappropriation of confidential business information, including financial information, trade secrets, financial loss and the disclosure of corporate strategic plans. The COVID-19 pandemic is generally increasing the attack surface available to criminals, as more companies and individuals work online and work remotely, and as such, the risk of a cybersecurity incident potentially occurring, and Tempest's investment in risk mitigations against such an incident, is increasing. For example, there has been an increase in phishing and spam emails as well as social engineering attempts from "hackers" hoping to use the recent COVID-19 pandemic to their advantage.

Although Tempest devotes resources to protect its information systems, Tempest realizes that cyberattacks are a threat, and there can be no assurance that Tempest's efforts will prevent information security breaches that would result in business, legal, financial or reputational harm to Tempest, or would have a material adverse effect on Tempest's results of operations and financial condition.

In addition, the computer systems of various third parties on which Tempest relies, including its CROs, CMOs and other contractors, consultants and law and accounting firms, may sustain damage from computer viruses, unauthorized access, data breaches, phishing attacks, cybercriminals, natural disasters (including hurricanes and earthquakes), terrorism, war and telecommunication and electrical failures. Tempest relies on its third-party providers to implement effective security measures and identify and correct for any such failures, deficiencies or breaches.

Tempest's employees, principal investigators, CROs, CMOs and consultants may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

Tempest is exposed to the risk of fraud or other misconduct by Tempest's employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of FDA and non-U.S. regulators, to provide accurate information to the FDA and non-U.S. regulators, to comply with healthcare fraud and abuse laws and regulations in the United States and abroad, to report financial information or data accurately or disclose unauthorized activities to Tempest. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical studies, which could result in regulatory sanctions and could cause serious harm to Tempest's reputation. It is not always possible to identify and deter employee misconduct, and the precautions Tempest takes to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting Tempest from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against Tempest, and Tempest is not successful in defending or asserting Tempest's rights, those actions could have a significant impact on Tempest's business, including the imposition of significant fines or other sanctions.

Tempest's business entails a significant risk of product liability and Tempest's ability to obtain sufficient insurance coverage could have a material and adverse effect on Tempest's business, financial condition, results of operations and prospects.

Tempest will face an inherent risk of product liability exposure related to the testing of its product candidates in clinical trials and will face an even greater risk if Tempest commercializes any of Tempest's product candidates. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in a product, negligence, strict liability or breach of warranty. Claims could also be asserted under U.S. state consumer protection acts. If Tempest cannot successfully defend Tempest's against claims that Tempest's product candidates caused injuries, Tempest could incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for any product candidates that Tempest may develop;
- injury to Tempest's reputation and significant negative media attention;
- withdrawal of clinical trial participants;

- significant time and costs to defend the related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- termination of Tempest's collaboration relationships or disputes with its collaborators;
- voluntary product recalls, withdrawals or labeling restrictions; and
- the inability to commercialize any product candidates that Tempest may develop.

While Tempest currently has insurance that Tempest believes is appropriate for Tempest's stage of development, Tempest may need to obtain higher levels prior to clinical development or marketing any of its future product candidates. Any insurance Tempest has or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, Tempest may be unable to obtain sufficient insurance at a reasonable cost to protect Tempest against losses caused by product liability claims that could have a material and adverse effect on Tempest's business, financial condition, results of operations and prospects.

Our ability to utilize our net operating loss carryforwards and tax credit carryforwards may be subject to limitations.

Our ability to use our federal and state net operating losses ("NOLs") to offset potential future taxable income and related income taxes that would otherwise be due is dependent upon our generation of future taxable income, and we cannot predict with certainty when, or whether, we will generate sufficient taxable income to use all of its NOLs.

Under Section 382 and Section 383 of the Code and corresponding provisions of state law, if a corporation undergoes an "ownership change," its ability to use its pre-change NOL carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income or taxes may be limited. A Section 382 "ownership change" is generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three-year period. We may have experienced ownership changes in the past, including as a result of the Merger, and may experience ownership changes in the future due to subsequent shifts in our stock ownership (some of which are outside of its control). Furthermore, the Merger, constituted an ownership change (within the meaning of Section 382 of the Code) of Millendo which may have eliminated or otherwise substantially limited our ability to use Millendo's federal and state NOLs to offset our future taxable income. Consequently, even if we achieve profitability, we may not be able to utilize a material portion of Tempest's, Millendo's or our combined NOL carryforwards and other tax attributes, which could have a material adverse effect on cash flow and results of operations. Similar provisions of state tax law may also apply to limit our ability to use of accumulated state tax attributes. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to offset future income tax liabilities.

Changes in tax laws or regulations could materially adversely affect us.

New tax laws or regulations could be enacted at any time, and existing tax laws or regulations could be interpreted, modified or applied in a manner that is adverse to us, which could adversely affect its business and financial condition. For example, legislation enacted in 2017, informally titled the Tax Act, enacted many significant changes to the U.S. tax laws, including changes in corporate tax rates, the utilization of NOLs and other deferred tax assets, the deductibility of expenses, and the taxation of foreign earnings. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various states will conform to the Tax Act, the CARES Act, or any newly enacted federal tax legislation. The impact of changes under the Tax Act, the CARES Act, or future reform legislation could increase our future U.S. tax expense and could have a material adverse impact on its business and financial condition.

The trading price of the shares of our common stock has been and is likely to continue to be volatile, and purchasers of our common stock could incur substantial losses.

The market price of our common stock has been and is likely to continue to be volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- results of clinical trials and preclinical studies of our product candidates, or those of our competitors or our existing or future collaborators;
- failure to meet or exceed financial and development projections we may provide to the public;
- failure to meet or exceed the financial and development projections of the investment community;
- if we do not achieve the perceived benefits of the Merger as rapidly or to the extent anticipated by financial or industry analysts;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- actions taken by regulatory agencies with respect to our product candidates, clinical studies, manufacturing process or sales and marketing terms;
- disputes or other developments relating to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for its technologies;
- additions or departures of key personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or if they issue adverse or misleading opinions regarding our business and stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions or market conditions in the pharmaceutical and biotechnology sectors;
- sales of securities by us or our securityholders in the future;
- if we fail to raise an adequate amount of capital to fund our operations and continued development of our product candidates;
- trading volume of our common stock;
- announcements by competitors of new commercial products, clinical progress or lack thereof, significant contracts, commercial relationships or capital commitments;
- adverse publicity relating to precision medicine product candidates, including with respect to other products in such markets;
- the introduction of technological innovations or new therapies that compete with our products and services; and
- period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock. In addition, a recession, depression or other sustained adverse market event resulting from the spread of COVID-19 or otherwise could materially and adversely affect our business and the value of our common stock. In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against such companies. Furthermore, market volatility may lead to increased shareholder activism if we experience a market valuation that activists believe is not reflective of its intrinsic value. Activist campaigns that contest or conflict with our strategic direction or seek changes in the composition of our board of directors could have an adverse effect on its operating results and financial condition.

Private Tempest and Millendo may be unable to integrate successfully and we may not realize the anticipated benefits of the Merger.

The Merger involves the combination of two companies which have operated as independent companies. We may fail to realize some or all of the anticipated benefits of the Merger if the integration process takes longer than expected or is more costly than expected. It is possible that the integration process also could result in the diversion of our management's attention, the disruption or interruption of, or the loss of momentum in, our ongoing businesses or inconsistencies in standards, controls, procedures and policies, any of which could adversely affect our ability to maintain relationships with customers, suppliers and employees or the ability to achieve the anticipated benefits of the Merger, or could otherwise adversely affect our business and financial results.

We expect to continue to incur increased costs as a result of operating as a public company, and our management is required to devote substantial time to compliance with our public company responsibilities and corporate governance practices.

As a relatively new public company, we continue to incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Capital Market and other applicable securities rules and regulations impose various requirements on public companies. Our management and other personnel need to devote a substantial amount of time to compliance with these requirements. Moreover, these rules and regulations increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain directors' and officers' liability insurance, compared to when we were a private company, which could make it more difficult for us to attract and retain qualified members of our board of directors. We cannot predict or estimate the amount of additional costs we will continue to incur as a public company or the timing of such costs. Once we are no longer a smaller reporting company or otherwise no longer qualifies for applicable exemptions, we will be subject to additional laws and regulations affecting public companies that will increase our costs and the demands on management and could harm our operating results.

Provisions in our certificate of incorporation and by-laws and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and by-laws may discourage, delay or prevent a merger, acquisition or other change in control of the company that stockholders may consider favorable, including transactions in which our common stockholders might otherwise receive a premium price for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that not all members of the board are elected at one time;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from the board;

- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and for nominations to our board of directors;
- limit who may call stockholder meetings;
- prohibit actions by our stockholders by written consent;
- require that stockholder actions be effected at a duly called stockholders meeting;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75 percent of the votes that all our stockholders would be entitled to cast to amend or repeal certain provisions of our certificate of incorporation or by-laws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns 15 percent or more of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired 15 percent or more of our outstanding voting stock, unless the merger or combination is approved in a manner prescribed by the statute.

Our bylaws provide that the Court of Chancery of the State of Delaware is the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or other employees.

Our bylaws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for any derivative action or proceeding brought on our behalf, any action asserting a breach of fiduciary duty, any action asserting a claim against it arising pursuant to any provisions of the DGCL, our certificate of incorporation or our bylaws, or any action asserting a claim against us that is governed by the internal affairs doctrine. The provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in the bylaws to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially and adversely affect our business, financial condition and results of operations.

We do not anticipate that we will pay any cash dividends in the foreseeable future.

The current expectation is that we will retain its future earnings, if any, to fund our growth as opposed to paying dividends. As a result, capital appreciation, if any, of our common stock will be your sole source of gain, if any, for the foreseeable future.

Future sales of shares by existing stockholders could cause our stock price to decline.

If our existing securityholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after legal restrictions on resale lapse, the trading price of our common stock could decline. As of June 30, 2021, of the total 6,637,081 shares of common stock outstanding, approximately 4,230,786 shares will be available for sale in the public market beginning 180 days after the closing of the Merger as a result of the expiration of lock-up agreements between Millendo and Private Tempest on the one hand and certain securityholders of Millendo and Private Tempest on the other hand. All other outstanding shares of common stock, other than shares held by our affiliates, will be freely tradable, without restriction, in the public market. In addition, shares of common stock that are subject to outstanding options of Tempest will become eligible for sale in the public market to the extent permitted by the provisions of various vesting agreements and Rules 144 and 701 under the Securities Act. If these shares are sold, the trading price of our common stock could decline.

Our executive officers, directors and principal stockholders have the ability to control or significantly influence all matters submitted to our stockholders for approval.

Our executive officers, directors and principal stockholders, in the aggregate, beneficially own approximately 65.8% of our outstanding shares of common stock. As a result, if these persons were to choose to act together, they would be able to control or significantly influence all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control or significantly influence the election of directors and approval of any merger, consolidation or sale of all or substantially all of the company's assets. This concentration of voting power could delay or prevent an acquisition on terms that other stockholders may desire.

We may be exposed to increased litigation, including stockholder litigation, which could have an adverse effect on our business and operations.

We may be exposed to increased litigation from stockholders, customers, suppliers, consumers and other third parties due to the combination of Millendo's business and Tempest's business following the merger. Such litigation may have an adverse impact on our business and results of operations or may cause disruptions to our operations. In addition, in the past, stockholders have initiated class action lawsuits against biotechnology companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

We also remain the subject of various securities class action lawsuits and shareholder derivative lawsuits that were filed against OvaScience and certain of its officer and directors, as described in more detail in Part II-Item 1 under the heading "Legal Proceedings" of our Quarterly Report on Form 10-Q for the quarter ended March 31, 2021.

If equity research analysts do not publish research or reports, or publish unfavorable research or reports, about us, our business or our market, our stock price and trading volume could decline.

The trading market for our common stock will be influenced by the research and reports that equity research analysts publish about us and our business. We have no control over the analysts or the content and opinions included in their reports. The price of our common stock could decline if one or more equity research analysts downgrade our stock or issue other unfavorable commentary or research. If one or more equity research analysts ceases coverage or fails to publish reports on us regularly, demand for our common stock could decrease, which in turn could cause its stock price or trading volume to decline.

Exhibit 99.3

TEMPEST MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion of our financial condition and results of operations in conjunction with our unaudited Interim Financial Statements and the notes thereto included on the Current Report on Form 8-K/A filed with the Securities and Exchange Commission ("SEC") on July 1, 2021. This discussion contains forward-looking statements that involve risks and uncertainties, such as its plans, objectives, expectations, intentions, and beliefs. Tempest's actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified in Exhibit 99.2 included on the Current Report on Form 8-K filed with the SEC on July 16, 2021.

Overview

Tempest is a clinical-stage oncology company focused on leveraging its deep scientific understanding of cancer biology and medicinal chemistry to develop and advance novel orally available therapies for the treatment of solid tumors. Tempest's philosophy is to build a company based upon not only good ideas and creative science, but also upon the efficient translation of those ideas into therapies that will improve patient's lives. To this end, Tempest is advancing TPST-1495 and TPST-1120, two product candidates in clinical trials that it believes are the first clinical stage molecules designed to treat their respective targets; and a third program in preclinical studies that could be the first to target TREX-1, a key cellular enzyme that regulates the innate immune response in tumors. TPST-1495 is a dual antagonist of EP2 and EP4, receptors of prostaglandin E2, and is currently in a Phase 1 trial in solid tumors. Tempest's second program, TPST-1120, is a selective antagonist of peroxisome proliferator-activated receptor alpha, or PPARα, and is also in a Phase 1 trial in solid tumors. Tempest expects to report initial data from both these programs in the second half of 2021. Additionally, Tempest is advancing a third program targeting the three prime repair exonuclease, or TREX-1, for which Tempest expects to select a development candidate by the end of 2021. Beyond these three ongoing programs, Tempest plans to leverage its drug development and company-building experience along with academic relationships to identify promising new targets that may feed new programs into Tempest's pipeline.

Tempest has no products approved for commercial sale and has not generated any revenue from product sales. From inception to March 31, 2021, Tempest has raised $115 million, through sales of convertible preferred stock and issuance of debt.

Tempest has never been profitable and has incurred operating losses in each period since inception. Tempest's net losses were $5.4 million and $4.2 million for the three months period ended March 31, 2021 and 2020, respectively. As of March 31, 2021, Tempest had an accumulated deficit of $77.1 million. Substantially all of its operating losses resulted from expenses incurred in connection with its research and development programs and from general and administrative costs associated with its operations.

Tempest expects to incur significant expenses and increasing operating losses for at least the next several years as it initiates and continues the clinical development of, and seeks regulatory approval for, its product candidates and adds personnel necessary to advance its pipeline of clinical-stage product candidates. In addition, operating as a publicly traded company will involve the hiring of additional financial and other personnel, upgrading its financial information and other systems, and incurring substantial costs associated with operating as a public company. Tempest expects that its operating losses will fluctuate significantly from quarter to quarter and year to year due to timing of clinical development programs and efforts to achieve regulatory approval.

As of March 31, 2021, Tempest had cash and cash equivalents of $27.4 million. Tempest's ability to fund continued development will require additional capital, and Tempest intends to raise such capital through the issuance of additional debt or equity including in connection with potential merger opportunities, or through business development activities. The ability of Tempest to continue as a going concern is dependent upon its ability to successfully accomplish these plans and secure sources of financing and ultimately attain profitable operations. If Tempest is unable to obtain adequate capital, it could be forced to cease operations.

Oxford Loan and Security Agreement

On January 15, 2021, Tempest entered into a loan and security agreement with Oxford Finance LLC ("Oxford") to borrow a term loan amount of $35.0 million to be funded in three tranches. Tranche A of $15.0 million was funded to Tempest on January 15, 2021. Tranche B of $10.0 million will be available through March 31, 2022 contingent upon achievement of each of the following: i) receipt of at least $50.0 million in Series C equity capital, ii) initiation of the Phase 1 combination study of TPST-1495 or monotherapy expansion study, and iii) initiation of Phase 2 trial of TPST-1120 or the 1L Triplet Collaboration study. And Tranche C of $10.0 million is available at Oxford's option. The term loan matures on August 1, 2025 and has an annual floating interest rate of 7.15% which is an Index Rate plus 7.15% which is an index rate plus 7%. The index rate is the greater of (i) 30-day US LIBOR or (ii) 0.15%.

Merger Agreement

On March 29, 2021, Tempest entered into an Agreement and Plan of Merger (the "Merger Agreement") with Millendo Therapeutics, Inc. Concurrent with the execution and delivery of the Merger Agreement, Tempest entered into funding agreements with certain investors named therein, pursuant to which the investors agreed to purchase, in the aggregate, $30.0 million of Tempest common stock convertible into securities of Millendo.

On June 25, 2021, Tempest closed the Merger Agreement with Millendo Therapeutics. Pursuant to the Merger Agreement, Mars Merger Corp. (or Merger Sub), a direct, wholly owned subsidiary of Millendo merged with and into Tempest, with Tempest surviving as a wholly owned subsidiary of Millendo. Before the closing of the merger, investors in the pre-closing financing purchased Tempest's common stock totaling $30 million. Following the closing of the merger, Millendo changed its corporate name to Tempest Therapeutics, Inc.

Financial Operations Overview

Research and Development Expense

Research and development expenses represent costs incurred to conduct research and development, such as the development of Tempest's product candidates. Tempest recognizes all research and development costs as they are incurred. Research and development expenses consist primarily of the following:

- salaries, benefits and stock-based compensation;
- licensing costs;
- allocated occupancy;
- materials and supplies;
- contracted research and manufacturing;
- consulting arrangements; and
- other expenses incurred to advance Tempest's research and development activities.

The largest component of Tempest's operating expenses has historically been the investment in research and development activities. Tempest expects research and development expenses will increase in the future as Tempest advances its product candidates into and through clinical trials and pursues regulatory approvals, which will require a significant investment in costs of clinical trials, regulatory support and contract manufacturing and inventory build-up. In addition, Tempest continues to evaluate opportunities to acquire or in-license other product candidates and technologies, which may result in higher research and development expenses due to license fee and/or milestone payments, as well as added clinical development costs.

The process of conducting clinical trials necessary to obtain regulatory approval is costly and time consuming. Tempest may never succeed in timely developing and achieving regulatory approval for its product candidates. The probability of success of Tempest's product candidates may be affected by numerous factors, including clinical data, competition, manufacturing capability and commercial viability. As a result, Tempest is unable to determine the duration and completion costs of Tempest's development projects or when and to what extent Tempest will generate revenue from the commercialization and sale of any of its product candidates.

General and Administrative Expenses

General and administrative expenses consist of employee-related expenses, including salaries, benefits, travel and noncash stock-based compensation, for the Tempest personnel in executive, finance and accounting, and other administrative functions, as well as fees paid for legal, accounting and tax services, consulting fees and facilities costs not otherwise included in research and development expense. Legal costs include general corporate legal fees and patent costs. Tempest expects to incur additional expenses as a result of becoming a public company following completion of the merger, including expenses related to compliance with the rules and regulations of the SEC and Nasdaq, additional insurance, investor relations and other administrative expenses and professional services.

Other Income (Expense), Net

Other income (expense), net consists primarily of interest expense, interest income, and various income or expense items of a non-recurring nature.

Results of Operations

Summary of the three months period ended March 31, 2021 and 2020

	Three months ended March 31, 2021	Three months ended March 31, 2020
		(in thousands)
Expenses:		
Research and development	$ 3,592	$ 3,027
General and administrative	1,538	1,276
Total expenses	5,130	4,303
Operating loss	(5,130)	(4,303)
Interest expense	(231)	—
Interest income and other income, net	3	75
Provision for income taxes	—	—
Net loss	$(5,358)	$ (4,228)

Research and development

Tempest's research and development expenses for the three months period ended March 31, 2021 and 2020 were primarily incurred in connection with Tempest's most advanced product candidates, TPST-1120 and TPST-1495. Tempest has not historically tracked research and development expense by program other than direct external expenses in conducting clinical trials for TPST-1120 and TPST-1495. Tempest typically has various early-stage research and drug discovery projects, as well as various potential product candidates undergoing clinical trials. Tempest's internal resources, employees and infrastructure are not directly tied to any one research and drug discovery project and Tempest's resources are typically deployed across multiple projects. As such Tempest does not maintain information regarding these costs incurred for these early-stage research and drug discovery programs on a project specific basis.

Research and development expense increased by $0.6 million to $3.6 million for the three months period ended March 31, 2021. The following table summarizes Tempest's research and development expenses for the three months period ended March 31, 2021 and 2020:

	Three Months Ended March 31,	
	2021	2020
	(in thousands)	
Research and development outside services	$ 2,113	$ 2,066
Compensation expense	790	475
Stock-based compensation expense		
Consulting and professional services	475	252
Other expenses	214	234
Total research and development expense	$ 3,592	$ 3,027

The growth in total research and development expense of $0.6 million for the three months period ended March 31, 2021 was attributable to increased compensation expenses and increased clinical development expense for TPST-1120 and TPST-1495. These increases were partially offset by decreased research and support service fees paid to a certain clinical services firm.

General and administrative

General and administrative expenses increased by $0.3 million to $1.5 million for the three months period ended March 31, 2021. The increase was primarily due to growth in compensation related expense.

Other income and expense

For the three months period ended March 31, 2021, total interest expense was $231 related to the Oxford Loan. There was no interest expense for the three months period ended March 31, 2020. Interest income was $3 and $75 for the three months period ended March 31, 2021 and 2020, respectively.

Liquidity and Capital Resources

Sources of Liquidity

Since inception through March 31, 2021, Tempest's operations have been financed primarily by net cash proceeds from the sale of its convertible preferred stock and issuance of debt. As of March 31, 2021, Tempest had $27.4 million in cash and cash equivalents and an accumulated deficit of $77.1 million. Tempest expects that its research and development and general and administrative expenses will increase, and, as a result, Tempest anticipates that it will continue to incur increasing losses in the foreseeable future. Therefore, Tempest will need to raise additional capital to fund its operations, which may be through the issuance of additional equity or through borrowings, including in connection with the merger, or through business development activities.

On January 15, 2021, Tempest entered into a loan and security agreement with Oxford Finance LLC ("Oxford") to borrow a term loan amount of $35.0 million to be funded in three tranches. Tranche A of $15.0 million was funded to Tempest on January 15, 2021. Tranche B of $10.0 million will be available through March 31, 2022 contingent upon achievement of each of the following: i) receipt of at least $50.0 million in Series C equity capital, ii) initiation of the Phase 1 combination study of TPST-1495 or monotherapy expansion study, and iii) initiation of Phase 2 trial of TPST-1120 or the 1L Triplet Collaboration study. And Tranche C of $10.0 million is available at Oxford's option. The term loan matures on August 1, 2025 and has an annual floating interest rate of 7.15% which is an Index Rate plus 7.15% which is an index rate plus 7%. The index rate is the greater of (i) 30-day US LIBOR or (ii) 0.15%.

On March 29, 2021, Tempest entered into an Agreement and Plan of Merger (the "Merger Agreement") with Millendo Therapeutics, Inc. Concurrent with the execution and delivery of the Merger Agreement, Tempest entered into funding agreements with certain investors named therein, pursuant to which the investors agreed to purchase, in the aggregate, $30.0 million of Tempest common stock convertible into securities of Millendo.

On June 25, 2021, Tempest closed the Merger Agreement with Millendo Therapeutics. Pursuant to the Merger Agreement, Mars Merger Corp. (or Merger Sub), a direct, wholly owned subsidiary of Millendo merged with and into Tempest, with Tempest surviving as a wholly owned subsidiary of Millendo. Before the closing of the merger, investors in the pre-closing financing purchased Tempest's common stock totaling $30 million. Following the closing of the merger, Millendo changed its corporate name to Tempest Therapeutics, Inc.

Cash Flows

The following table summarizes Tempest's cash flows for the three months period indicated:

	Three Months Ended March 31,2021	Three Months Ended March 31, 2020
		(in thousands)
Cash used in operating activities	$ (6,276)	$ (5,477)
Cash used in investing activities	(14)	32
Cash provided by financing activities	14,910	34,558
Net increase in cash and cash equivalents	$ 8,620	$ 29,113

Cash flows from operating activities

Cash used in operating activities for the three months period ended March 31, 2021 was $6.3 million, consisting of a net loss of $5.4 million, add back of non-cash adjustments for depreciation, stock-based compensation, non-cash operating lease expense and other non-cash items totaling $0.3 million, less changes in operating assets and liabilities of $1.2 million.

Cash used in operating activities for the three months period ended March 31, 2020 was $5.5 million consisting of a net loss of $4.2 million, add back of non-cash adjustments for depreciation, stock-based compensation, non-cash operating lease expense and other non-cash items totaling $0.2 million, less changes in operating assets and liabilities of $1.5 million.

Cash flows from investing activities

Cash used in investing activities for the three months period ended March 31, 2021 was related to purchases of property and equipment, primarily related to office, laboratory and computer equipment. Cash provided by investing activities for the three months period ended March 31, 2020 was due to a repayment of a promissory note.

Cash flows from financing activities

Cash provided by financing activities for the three months period ended March 31, 2021 was primarily related to proceeds from the Oxford Loan of $14.9 million (net of issuance costs). Cash provided by financing activities for the three months period ended March 31, 2020 was primarily related to proceeds from the issuance of Series B-1 preferred stock of $34.5 million (net of issuance costs).

Future Funding Requirements

Tempest has not generated any revenue from product sales, and does not know when, or if, it will generate any revenue from product sales. Tempest does not expect to generate any revenue from product sales unless and until it obtains regulatory approval of and commercializes any of its product candidates. At the same time, Tempest expects its expenses to increase in connection with its ongoing development activities, particularly as Tempest continues the research, development and clinical trials of, and seeks regulatory approval for, its product candidates. In addition, subject to obtaining regulatory approval of any of its product candidates, Tempest anticipates that it will need substantial additional funding in connection with its continuing operations. Tempest plans to continue to fund its operations and capital requirements through equity financing, debt financing and/or business development activities, but there are no assurances that Tempest will be able to raise sufficient amounts of funding in the future on acceptable terms, or at all.

On January 15, 2021, Tempest entered into a loan and security agreement with Oxford Finance LLC ("Oxford") to borrow a term loan amount of $35.0 million to be funded in three tranches. Tranche A of $15.0 million was funded to Tempest on January 15, 2021. Tranche B of $10.0 million will be available through March 31, 2022 contingent upon achievement of each of the following: i) receipt of at least $50.0 million in Series C equity capital, ii) initiation of the Phase 1 combination study of TPST-1495 or monotherapy expansion study, and iii) initiation of Phase 2 trial of TPST-1120 or the 1L Triplet Collaboration study. And Tranche C of $10.0 million is available at Oxford's option. The term loan matures on August 1, 2025 and has an annual floating interest rate of 7.15% which is an Index Rate plus 7.15% which is an index rate plus 7%. The index rate is the greater of (i) 30-day US LIBOR or (ii) 0.15%.

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Until Tempest can generate a sufficient amount of product revenue to finance its cash requirements, it expects to finance its future cash needs primarily through the issuance of additional equity, borrowings and strategic alliances with partner companies. To the extent that Tempest raises additional capital through the issuance of additional equity or convertible debt securities, the ownership interest of Tempest's stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of existing stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting Tempest's ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If Tempest raises additional funds through marketing and distribution arrangements or other collaborations, strategic alliances or licensing arrangements with third parties, Tempest may have to relinquish valuable rights to its technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to Tempest. If Tempest is unable to raise additional funds through equity or debt financings when needed, Tempest may be required to delay, limit, reduce or terminate its product development or commercialization efforts or grant rights to develop and market product candidates to third parties that Tempest would otherwise prefer to develop and market itself.

Other Contracts

Tempest enters into contracts in the normal course of business with various third parties for preclinical research studies, clinical trials, testing and other services. These contracts generally provide for termination upon notice, and therefore Tempest believes that its non-cancelable obligations under these agreements are not material.

Off-Balance Sheet Arrangements

Tempest has not entered into any off-balance sheet arrangements and does not have any holdings in variable interest entities.

Quantitative and Qualitative Disclosures about Market Risk

Tempest is exposed to market risks in the ordinary course of its business. These risks primarily include interest rate fluctuation. As of March 31, 2021, and December 31, 2020, Tempest had cash and cash equivalents of approximately $27.4 million and $18.8 million, respectively, which consisted primarily of bank deposit and money market funds. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations of interest income have not been significant.

Critical Accounting Polices and Estimates

Tempest's management's discussion and analysis of financial condition and results of operations is based on its financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these financial statements requires Tempest to make estimates and judgments that affect the reported amounts of assets, liabilities and expenses. On an ongoing basis, Tempest evaluates these estimates and judgments. Tempest bases its estimates on historical experience and on various assumptions that Tempest believes to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities and the recording of expenses that are not readily apparent from other sources. Actual results may differ materially from these estimates. Tempest believes that the accounting policies discussed below are critical to understanding its historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Accrued Research and Development Expenses

Tempest records accrued expenses for estimated costs of its research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials and contract manufacturing activities. Tempest records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and Tempest includes these costs in accrued liabilities in the balance sheets and within research and development expense in the statement of operations. These costs are a significant component of Tempest's research and development expense. Tempest records accrued expenses for these costs based on the estimated amount of work completed and in accordance with agreements established with these third parties.

Tempest estimates the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. Tempest makes significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, Tempest adjusts its accrued estimates. Although Tempest does not expect its estimates to be materially different from amounts actually incurred, Tempest's understanding of the status and timing of services performed, the number of patients enrolled and the rate of patient enrollment may vary from its estimates and could result in Tempest reporting amounts that are too high or too low in any particular period. Tempest's accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers.

Fair Value of Common Stock

The fair values of the shares of common stock underlying the share-based awards were estimated on each grant date by the board of directors. Tempest used the option-pricing method (OPM). Under the OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The estimated fair values of the preferred and common stock are inferred by analyzing these options. Tempest applied a discount for lack of marketability to account for a lack of access to an active public market.

Application of this approach involves the use of estimates, judgment, and assumptions that are complex and subjective, such as those regarding the expected future revenue, expenses, and cash flows, discount rates, market multiples, the selection of comparable companies, and the probability of future events. Changes in any or all of these estimates and assumptions, or the relationships between those assumptions, impact the valuation and may have a material impact on the valuation of common stock which is the key input into the calculation of stock-based compensation.

Stock-based Compensation

Tempest recognizes noncash stock-based compensation expense related to stock-based awards to employees, non-employees and directors, including stock options, based on the fair value on the grant date using the Black-Scholes option pricing model. The related stock-based compensation is recognized as expense on a straight line-basis over the employee's, non-employee's or director's requisite service period (generally the vesting period). Noncash stock compensation expense is based on awards ultimately expected to vest and is reduced by an estimate for future forfeitures.

In determining the fair value of stock options, Tempest uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Fair Value of Common Stock—The fair value of the shares of common stock underlying stock options has historically been determined by Tempest's board of directors. Because there has been no public market for its common stock, the board of directors exercises reasonable judgment and considers a number of objective and subjective factors to determine the best estimate of the fair value of Tempest's common stock, including important developments in its operations, sales of redeemable convertible preferred stock, actual operating results and financial performance, the conditions in the life sciences industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of its common stock, among other factors.

Expected Term—Tempest's expected term represents the period that the stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term) for employee options.

Expected Volatility—Since Tempest is privately held and does not have any trading history for its common stock, the expected volatility is estimated based on the average volatility for comparable publicly traded biotechnology companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, or stage in the product development life cycle.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—Tempest has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, Tempest uses an expected dividend yield of zero.

For the three months period ended March 31, 2021 and 2020, stock-based compensation expense was $120 thousand and $3 thousand, respectively. Of the amount of $120 thousand in stock-based compensation expense, $77 thousand was recorded in research and development and $43 thousand was recorded in general and administrative for the three months period ended March 31, 2021. Of the amount of $3 thousand in stock-based compensation expense, $55 thousand was recorded in research and development and a credit of $52 thousand was recorded in general and administrative for the three months period ended March 31, 2020.

As of March 31, 2021, Tempest had $1.2 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which it expects to recognize over a weighted-average period of 1.5 years.

Exhibit 99.4

INDEX TO FINANCIAL STATEMENTS

TEMPEST THERAPEUTICS, INC.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the shareholders and the Board of Directors of Tempest Therapeutics Inc.

Opinion on the Financial Statements

We have audited the accompanying balance sheets of Tempest Therapeutics Inc. (the "Company") as of December 31, 2020 and 2019, the related statements of operations, convertible preferred stock and stockholders' deficit, and cash flows, for the years then ended, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2020 and 2019, and the results of its operations and its cash flows for the years then ended, in conformity with accounting principles generally accepted in the United States of America.

Going Concern

The accompanying financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the financial statements, the Company has incurred losses since inception and has forecasted cash needs in excess of current liquidity, which raises substantial doubt about its ability to continue as a going concern. Management's plans in regard to these matters are also described in Note 1. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB and in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Research and Development Expenses, Accrued Clinical Trial Liability, and Prepaid Research and Development Costs -Refer to Note 2 and Note 5 to the financial statements

Critical Audit Matter Description

The Company recognizes research and development expenses as incurred. Advance payments for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed. The Company recognizes its preclinical studies and clinical trial expenses based on the services performed pursuant to contracts with research institutions and clinical research organizations (collectively, "CRO") that conduct and manage preclinical studies and clinical trials on the Company's behalf. Service fees are accrued based on the Company's estimates of the time period over which services will be performed and the level of effort to be expended in each period. Total research and development expenses for the year ended December 31, 2020 was $14.4 million. Prepaid research and development costs as of December 31, 2020 was $0.4 million and the accrued clinical trial liability as of December 31, 2020 was $0.2 million.

At each balance sheet date, the Company estimates prepaid research and development costs and the accrued clinical trial liability by obtaining reporting from CROs, discussing progress or stage of completion of services with internal personnel and external service providers, and comparing this information to payments made, invoices received, and the agreed-upon fee to be paid for such services in the applicable contract, statements of work, or purchase orders. The estimate of the amount of work completed is primarily based on the status and timing of services performed, the number of patients enrolled, and the rate of patient enrollment.

We identified research and development expenses, accrued clinical trial liability, and prepaid research and development costs as a critical audit matter given the estimation involved in accounting for research and development expenses, accrued clinical trial liability, and prepaid research and development costs, as well as the material weaknesses identified by the Company in its internal controls over financial reporting. This required extensive audit effort related to the estimation of research and development expenses, accrued clinical trial liability and prepaid research and development costs.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to research and development expenses, accrued clinical trial liability and prepaid research and development costs included the following, among others:

- We selected a sample of amounts recognized as research and development expense, the accrued clinical trial liability and prepaid research development expenses and performed the following procedures for each item selected:
  - We obtained and read related master service agreements, statements of work, purchase orders or other supporting agreements with the CRO.
  - We performed corroborating inquiries with Company's clinical operations personnel responsible for the oversight of the activities regarding the nature and status of work performed.
  - We inspected evidence from the third-party vendor regarding the payments made and the status and timing of services performed, the number of patients enrolled, and the rate of patient enrollment incurred to date as well as payment information.
  - We compared the data and evidence obtained from internal and external sources to the inputs used in the Company's analysis and recalculated the related research and development expense, prepaid research and development expense, and the accrued clinical liability balances.
  - We tested the completeness and accuracy of the underlying data.
  - We evaluated management's judgments regarding status and timing of services performed, the number of patients enrolled, and the rate of patient enrollment compared to the evidence obtained.

- We examined a selection of subsequent payments and the related invoices to determine whether the related research and development expenses were appropriately recorded.

As a result of the material weaknesses, we increased the number of selections we would have otherwise made if the Company's controls were effective.

/s/ Deloitte & Touche LLP

San Francisco, California
May 10, 2021

We have served as the Company's auditor since 2017.

TEMPEST THERAPEUTICS, INC.

BALANCE SHEETS
AS OF DECEMBER 31, 2020 AND 2019
(in thousands except share and per share amounts)

	2020	2019
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 18,820	$ 3,244
Prepaid expenses and other current assets	1,005	519
Total current assets	19,825	3,763
PROPERTY AND EQUIPMENT—Net	1,110	1,400
OPERATING LEASE RIGHT OF USE ASSETS	1,877	2,353
OTHER NONCURRENT ASSETS	51	51
Total noncurrent assets	3,038	3,804
TOTAL ASSETS	$ 22,863	$ 7,567
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
CURRENT LIABILITIES:		
Accounts payable	$ 1,071	$ 1,645
Accrued liabilities	665	1,262
Current operating lease liability	712	33
Accrued compensation	695	447
Early option exercise liability	79	241
Total current liabilities	3,222	3,628
LONG TERM LIABILITIES:		
Operating lease liability	1,727	2,331
Total liabilities	4,949	5,959
COMMITMENTS AND CONTINGENCIES (Note 7)		
CONVERTIBLE PREFERRED STOCK, $0.001 PAR VALUE, 135,936,731 AND 147,231,000 SHARES AUTHORIZED AT DECEMBER 31, 2020 AND 2019, RESPECTIVELY; 114,686,731 and 70,936,735 SHARES ISSUED AND OUTSTANDING AT DECEMBER 31, 2020 AND 2019, RESPECTIVELY, LIQUIDATION PREFERENCE OF $100,186,732 and $65,186,736 AT DECEMBER 31, 2020 AND 2019, RESPECTIVELY	86,707	51,972
STOCKHOLDERS' EQUITY (DEFICIT):		
Common stock, $0.001 par value; 196,000,000 and 185,007,408 shares authorized; 16,374,711 and 15,939,555 issued and outstanding, 900,509 and 3,193,307 subject to repurchase at December 31, 2020 and 2019, respectively	15	13
Additional paid-in capital	2,953	2,176
Accumulated deficit	(71,761)	(52,553)
Total stockholders' deficit	(68,793)	(50,364)
TOTAL LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY	$ 22,863	$ 7,567

See accompanying notes to financial statements.

TEMPEST THERAPEUTICS, INC.

STATEMENTS OF OPERATIONS
FOR THE YEARS ENDED DECEMBER 31, 2020 AND 2019
(in thousands except share and per share amounts)

	2020	2019
EXPENSES:		
Research and development	$ 14,389	$ 17,867
General and administrative	4,909	5,507
Total expenses	19,298	23,374
OPERATING LOSS	(19,298)	(23,374)
OTHER INCOME:		
Change in fair value of convertible preferred stock tranche liability	—	8,746
Interest income	90	264
Total other income	90	9,010
PROVISION FOR INCOME TAXES	—	(1)
NET LOSS	$ (19,208)	$ (14,365)
Weighted average common shares outstanding - basic and diluted	14,539,178	12,578,207
Net loss per share attributable to common stockholders - basic and diluted	$ (1.32)	$ (1.14)

See accompanying notes to financial statements.

TEMPEST THERAPEUTICS, INC.

STATEMENTS OF CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' DEFICIT
FOR THE YEARS ENDED DECEMBER 31, 2020 AND 2019
(in thousands except share amounts)

	Series A Convertible Preferred Stock		Series B Convertible Preferred Stock		Series B1 Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Deficit Accumulated	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount			
BALANCE—January 1, 2019	17,000,000	$ 16,982	25,186,738	$ 12,235	—	$ —	9,935,448	$ 10	$ 1,494	$ (38,188)	$ (36,684)
Exercise of options—net of repurchase liability	—	—	—	—	—	—	288,693	—	44	—	44
Issuance of preferred stock for cash—net of issuance costs of $245	—	—	—	—	28,749,997	22,755	—	—	—	—	—
Vesting of early exercised stock options and restricted stock	—	—	—	—	—	—	2,522,107	3	328	—	331
Share-based compensation	—	—	—	—	—	—	—	—	310	—	310
Net loss	—	—	—	—	—	—	—	—	—	(14,365)	(14,365)
BALANCE—December 31, 2019	17,000,000	16,982	25,186,738	12,235	28,749,997	22,755	12,746,248	13	2,176	(52,553)	(50,364)
Exercise of options—net of repurchase liability	—	—	—	—	—	—	447,379	—	68	—	68
Issuance of preferred stock for cash—net of issuance costs of $265	—	—	—	—	43,749,996	34,735					
Vesting of early exercised stock options and restricted stock	—	—	—	—	—	—	2,280,575	2	256	—	258
Share-based compensation	—	—	—	—	—	—	—	—	453	—	453
Net loss	—	—	—	—	—	—	—	—	—	(19,208)	(19,208)
BALANCE—December 31, 2020	17,000,000	$ 16,982	25,186,738	$ 12,235	72,499,993	$57,490	15,474,202	$ 15	$ 2,953	$ (71,761)	$ (68,793)

See accompanying notes to financial statements.

TEMPEST THERAPEUTICS, INC.

STATEMENTS OF CASH FLOWS
FOR THE YEARS ENDED DECEMBER 31, 2020 AND 2019
(in thousands)

	2020	2019
OPERATING ACTIVITIES:		
Net loss	$(19,208)	$(14,365)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	339	104
Stock based compensation	453	310
Noncash related party interest income	(6)	—
Noncash operating lease expense	476	444
Change in fair value of convertible preferred stock tranche liability	—	(8,746)
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(367)	(219)
Accounts payable	(574)	954
Operating lease liability	75	(433)
Accrued liabilities	(205)	392
Net cash used in operating activities	(19,017)	(21,559)
INVESTING ACTIVITIES:		
Purchase of property and equipment	(50)	(1,364)
Repayment of related party note receivable	44	—
Net cash used in investing activities	(6)	(1,364)
FINANCING ACTIVITIES:		
Proceeds from issuance of Series B-1 convertible preferred stock	35,000	23,000
Payment of preferred stock issuance costs	(469)	(41)
Exercise of stock options	69	44
Repurchase of non vested options	(1)	—
Net cash provided by financing activities	34,599	23,003
NET INCREASE IN CASH AND CASH EQUIVALENTS	15,576	80
CASH AND CASH EQUIVALENTS —Beginning of year	3,244	3,164
CASH AND CASH EQUIVALENTS —End of year	$ 18,820	$ 3,244
SUPPLEMENTAL DISCLOSURE FOR CASH FLOW ACTIVITIES—Cash paid for income taxes	$ —	$ 1
NON-CASH OPERATING ACTIVITIES—Operating lease right-of-use asset recorded on adoption of ASC 842	$ —	$ 2,798
NON-CASH INVESTING ACTIVITIES—Property and equipment in accounts payable	$ —	$ 84
NON-CASH FINANCING ACTIVITIES:		
Issuance costs for issuance of Series B-1 Preferred Stock in accrued liabilities	$ —	$ 204
Debt issuance costs related to financing in accrued liabilities	$ 34	$ —
Vesting of early exercise stock options	$ 258	$ 330

See accompanying notes to financial statements.

1. DESCRIPTION OF THE BUSINESS

Nature of Business—Tempest Therapeutics (the Company) was incorporated in the state of Delaware on February 10, 2011 originally as Next Beta, Inc., and then changed its name to Inception 2, Inc. on October 4, 2011 and then finally to Tempest Therapeutics, Inc. on August 14, 2017. The Company is a privately held, small biopharmaceutical company focused on the discovery and development of small molecule drugs to treat cancers such as hepatocellular carcinoma and colorectal cancer. The Company is headquartered in South San Francisco, California.

Liquidity and Management Plans—The accompanying financial statements have been prepared assuming the Company will continue as a going concern. In the course of its development activities, the Company has incurred significant losses since inception, including a net loss of approximately $19.2 million and $14.4 million for the years ended December 31, 2020 and 2019, respectively, and expects such losses to continue for the foreseeable future. As of December 31, 2020, and 2019, the Company had cash and cash equivalents of approximately $18.8 million and $3.2 million, respectively, and accumulated deficit of approximately $71.8 million and has forecasted cash needs in excess of current liquidity. To date, the Company has funded its operations primarily with the net proceeds from the sale of convertible preferred stock and convertible preferred notes. As a result of these conditions, substantial doubt is raised about the Company's ability to continue as a going concern within one year after the date that the financial statements are available to be issued.

The Company is continuing to develop its drug candidates, which is the primary use of funds for the Company. The Company's ability to fund continued development will require additional capital, and the Company intends to raise such capital through the issuance of additional debt or equity including in connection with potential merger opportunities, or through business development activities. As described in Note 14, on March 29, 2021, Tempest entered into an Agreement and Plan of Merger (the "Merger Agreement") with Millendo Therapeutics, Inc. Concurrent with the execution and delivery of the Merger Agreement, Tempest entered into funding agreements with certain investors named therein, pursuant to which the investors agreed to purchase, in the aggregate, $30.0 million of Tempest common stock convertible into securities of Millendo. However, if such financing is not approved, does not occur, or alternative financing is not available at adequate levels or on acceptable terms, the Company could be required to significantly reduce operating expenses and delay, reduce the scope of or eliminate some of its development programs, enter into a collaboration or other similar arrangement with respect to commercialization rights to any of its product candidates, out-license intellectual property rights to its product candidates and sell unsecured assets, or a combination of the above. Any of these actions could have a material adverse effect on the Company's business, results of operations, financial condition and/or its ability to fund its scheduled obligations on a timely basis or at all. The ability of the Company to continue as a going concern is dependent upon its ability to successfully accomplish these plans and secure sources of financing and ultimately attain profitable operations. If the Company is unable to obtain adequate capital, it could be forced to cease operations.

These plans are intended to mitigate the relevant conditions or events that raise substantial doubt about the Company's ability to continue as a going concern; however, as the plans are not entirely within the Company's control, management has determined it is not probable they will be effectively implemented. The accompanying financial statements do not include any adjustments that might be necessary if the Company is unable to continue as a going concern.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation—The financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP).

Use of Estimates—The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of expenses during the reporting period. On an ongoing basis, the Company evaluates its estimates and assumptions, including those related to research and development accruals, recoverability of long-lived assets, right-of-use assets, lease obligations, fair value of convertible preferred stock tranche liability, fair value of common stock stock-based compensation and income taxes uncertainties and valuation allowances. Management bases its estimates on historical experience and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from those estimates.

Segment Information – The Company operates and manages its business as one reportable and operating segment, which is the business of discovery and development of small molecule drugs to treat cancers. All assets and operations are in the U.S. The Company's Chief Executive Officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance.

Risks and Uncertainties – The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including, but not limited to, development by competitors of new technological innovations, protection of proprietary technology, dependence on key personnel, reliance on single-source vendors, availability of raw materials, patentability of the Company's products and processes and clinical efficacy and safety of the Company's products under development, compliance with government regulations and the need to obtain additional financing to fund operations. Product candidates currently under development will require significant additional research and development efforts, including extensive preclinical studies, clinical trials and regulatory approval, prior to commercialization. These efforts will require significant amounts of additional capital, adequate personnel infrastructure and extensive compliance and reporting. The Company's product candidates are still in development and, to date, none of the Company's product candidates have been approved for sale and, therefore, the Company has not generated any revenue from product sales. There can be no assurance that the Company's research and development will be successfully completed, that adequate protection for the Company's intellectual property will be obtained or maintained, that any products developed will obtain necessary government regulatory approval or that any approved products will be commercially viable. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will generate revenue from product sales. The Company operates in an environment of rapid technological change and substantial competition from other pharmaceutical and biotechnology companies. In addition, the Company is dependent upon the services of its employees, consultants and other third parties.

Moreover, the current COVID-19 (coronavirus) pandemic, which is impacting worldwide economic activity, poses risk that the Company or its employees, contractors, suppliers, and other partners may be prevented from conducting business activities for an indefinite period of time, including due to shutdowns that may be requested or mandated by governmental authorities. The extent to which the COVID-19 pandemic will impact the Company's business will depend on future developments that are highly uncertain and cannot be predicted at this time.

Concentration of Credit Risk—Financial instruments, which potentially subject the Company to concentration of risk, consist principally of cash and money market fund. All of the Company's cash and money market fund are deposited in accounts with a major financial institution, and amounts may exceed federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial strength of the depository institution in which the cash and money market fund are held. The

Company has no off-balance sheet concentrations of credit risk, such as foreign currency exchange contracts, option contracts or other hedging arrangements.

Cash and Cash Equivalents—The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisitions to be cash equivalents. As of December 31, 2020, and 2019, the Company's cash and cash equivalents consisted of bank deposits and a money market fund.

Property and Equipment—Property and equipment is recorded at cost and depreciated over the estimated useful lives of the related assets using the straight-line method. Upon disposal of an asset, the related cost and accumulated depreciation are removed from the asset accounts and any resulting gain or loss is included in the statement of operations. Repair and maintenance costs are expensed as incurred, whereas major improvements are capitalized as additions to property and equipment. The estimated useful lives of the Company's respective assets are as follows:

Computer equipment and software	3 years
Furniture and fixtures	7 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of the useful life of the asset or the life of the lease

Impairment of Long-Lived Assets—Long-lived assets are reviewed for impairment if events or circumstances indicate the carrying amount of these assets may not be recoverable. If this review indicates that these assets will not be recoverable, based on the forecasted undiscounted future operating cash flows expected to result from the use of long-lived assets and their eventual disposition, the Company's carrying value of the long-lived assets is reduced to fair value based on a discounted future cash flow approach or quoted market values. During 2020 and 2019, there were no events or circumstances which required an impairment test of long-lived assets.

Leases—The Company elected to early adopt Accounting Standard Update (ASU) No. 2016-02, *Leases* (ASC 842) and its associated amendments as of January 1, 2019 using the modified retrospective transition approach. There was no cumulative-effect adjustment recorded to accumulated deficit upon adoption.

Under ASC 842, the Company determines if an arrangement is a lease at inception. In addition, the Company determines whether leases meet the classification criteria of a finance or operating lease at the lease commencement date considering: (1) whether the lease transfers ownership of the underlying asset to the lessee at the end of the lease term, (2) whether the lease contains a bargain purchase option, (3) whether the lease term is for a major part of the remaining economic life of the underlying asset, (4) whether the present value of the sum of the lease payments and residual value guaranteed by the lessee equals or exceeds substantially all of the fair value of the underlying asset, and (5) whether the underlying asset is of such a specialized nature that it is expected to have no alternative use to the lessor at the end of the lease term. As of December 31, 2020 and 2019, the Company's lease population consisted only of an office lease. As of the date of adoption of ASC 842 and December 31, 2019, the Company did not have finance leases. Operating leases are included in operating lease right-of-use ("ROU") assets and operating lease liabilities in the balance sheet.

ROU assets represent the right to use an underlying asset for the lease term, and lease liabilities represent the obligation to make lease payments arising from the lease. Operating lease ROU assets and liabilities are recognized at lease commencement date based on the present value of lease payments over the lease term. The Company uses the implicit rate when readily determinable. If the Company's leases do not provide an implicit rate, an incremental borrowing rate is used based on the information available at commencement dates in determining the present value of lease payments. The determination of the Company's incremental borrowing rate requires management judgment including the development of a synthetic credit rating and cost of debt as the Company currently does not carry any debt. The incremental borrowing rate is estimated on a collateralized basis with similar terms and economic considerations under a recovery rate approach utilizing the historical recoverability rate of secured versus unsecured senior corporate debt to reflect a

recoverability-adjusted spread and overall rate on a lease by lease basis. The operating lease ROU assets also include any lease payments made and exclude lease incentives when paid by the Company or on the Company's behalf. The Company's lease terms may include options to extend or terminate the lease when it is reasonably certain that it will exercise that option. Lease expense for lease payments is recognized on a straight-line basis over the lease term.

The Company elected the practical expedient option that allows the Company to not need to reassess whether any expired or existing contracts are or contain leases, the lease classification for any expired or existing leases, and the initial direct costs for any existing leases. The Company elected the practical expedient to adopt the policy to not separate lease and non-lease components for its real estate leases. Operating leases are included in operating lease ROU assets and operating lease liabilities on the Company's balance sheets. The Company also made an accounting policy election to recognize lease expense for leases with a term of 12 months or less on a straight-line basis over the lease term and not recognize ROU assets or lease liabilities for such leases.

The Company has a lease for its office facility, which is classified as an operating lease. This lease has a lease term of five years, which includes an option to extend the lease. The Company has determined that it is not reasonably certain to exercise the option. The lease for the office includes costs for common area maintenance expenditures which are variable and not included in lease payments measured at lease inception. Differences between lease payments as measured at lease inception and variations in monthly payments will be recognized as operating expenses in the period in which the obligation is incurred. Please refer to Note 7 Commitments and Contingencies for details.

Convertible Preferred Stock—The Company records convertible preferred stock at fair value on the dates of issuance, net of issuance costs. The convertible preferred stock is recorded outside of stockholders' deficit because the shares contain liquidation features that are not solely within the Company's control. The Company has elected not to adjust the carrying values of the convertible preferred stock to the liquidation preferences of such shares because it is uncertain whether or when an event would occur that would obligate the Company to pay the liquidation preferences to holders of shares of convertible preferred stock. Subsequent adjustments to the carrying values to the liquidation preferences will be made only when it becomes probable that such a liquidation event will occur.

Convertible Preferred Stock Liability—The obligation to issue additional shares of the Company's Series B-1 convertible preferred stock at a future date was determined to be a freestanding financial instrument that should be accounted for as a liability. At initial recognition, the Company recorded the convertible preferred stock liability on the balance sheet at its estimated fair value. The liability is subject to remeasurement at each balance sheet date, with changes in fair value recognized as a gain or (loss) on remeasurement of convertible preferred stock liability on the statement of operations. The Company recognized a gain of $8.7 million associated with the change in fair value of preferred stock liability for the period ended December 31, 2019. In 2020, there was no such gain or loss. The convertible preferred stock liability balance was zero as of December 31, 2020 and 2019.

Comprehensive Loss—Comprehensive loss includes net loss as well as other changes in stockholders' deficit that results from transactions and economic events other than those with stockholders. There was no other comprehensive income or loss for the years ended December 31, 2020 and 2019.

Research and Development Expenses and Accrued Research and Development—Research and development expenses are charged to expense as incurred. Research and development expenses include certain payroll and personnel expenses, laboratory supplies, consulting costs, external contract research and development expenses. In-licensing fees and other costs to acquire technologies that are utilized in research and development, and that are not expected to have alternative future use, are expensed when incurred. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

The Company estimates preclinical studies and clinical trial expenses based on the services performed pursuant to contracts with research institutions and clinical research organizations that conduct and manage preclinical studies and clinical trials on the Company's behalf. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. These estimates are based on communications with the third-party service providers, the Company's estimates of accrued expenses and on information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies from the estimate, the Company will adjust the accrual accordingly. The estimates are trued up to reflect the best information available at the time of the financial statement issuance. Although the Company does not expect its estimates to be materially different from amounts actually incurred, the Company's estimate of the status and timing of services performed relative to the actual status and timing of services performed may vary.

Patent Costs – Costs related to filing and pursuing patent applications are expensed as incurred, as recoverability of such expenditures is uncertain. These patent related legal costs are reported as a component of general and administrative expense.

General and Administrative Expense – General and administrative costs are expensed as incurred and include employee-related expenses including salaries, benefits, travel and stock-based compensation for the Company's personnel in executive, finance and accounting, and other administrative functions, as well as fees paid for legal, accounting and tax services, consulting fees and facilities costs not otherwise included in research and development expense. Legal costs include general corporate legal fees and patent costs.

Fair Value Measurements—Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. The carrying amounts of the Company's financial instruments, including cash, prepaid and other current assets, accounts payable, accrued expenses and other liabilities approximate fair value due to their short-term maturities.

Stock-Based Compensation Expense—The Company accounts for stock-based compensation by measuring and recognizing compensation expense for all share-based payments made to employees, directors and non-employees based on estimated grant-date fair values. The Company uses the straight-line method to allocate compensation cost to reporting periods over each optionee's requisite service period, which is generally the vesting period.

The Company estimates the fair value of stock options to employees, directors and non-employees using the Black-Scholes option-valuation model. The Black-Scholes model requires the input of subjective assumptions, including expected volatility, expected dividend yield, expected term, risk-free rate of return, and the estimated fair value of the underlying common stock on the date of grant. Due to the lack of company-specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar companies that are publicly traded. The historical volatility is calculated based on a period of time commensurate with the expected term assumption. The group of representative companies have characteristics similar to the Company, including stage of product development and focus on the life science industry. The Company uses the simplified method to calculate the expected term for options granted to employees as it does not have sufficient historical exercise data to provide a reasonable basis upon which to estimate the expected term. The simplified method is based on the vesting period and the contractual term for each grant, or for each vesting tranche for awards with graded vesting. The mid-point between the vesting date and the maximum contractual expiration date is used as the expected term under this method. For awards with multiple vesting-tranches, the times from grant until the mid-points for each of the tranches may be averaged to provide an overall expected term. The risk-free interest rate is based on a treasury instrument whose term is consistent with the expected term of the stock options. The Company uses an assumed dividend yield of zero as the Company has never paid dividends and has no current plans to pay any dividends on its common stock.

The Company accounts for forfeitures as they occur. The fair value of restricted stock awards granted to employees are valued as of the grant date using the estimated fair value of the Company's common stock.

Net Loss per Share Attributable to Common Stockholders—The Company follows the two-class method when computing net loss per share as the Company has issued shares that meet the definition of participating securities. The two-class method determines net loss per share for each class of common and participating securities according to dividends declared or accumulated and participation rights in undistributed earnings. The two-class method requires income available to common stockholders for the period to be allocated between common and participating securities based upon their respective rights to receive dividends as if all income for the period had been distributed.

Basic net loss per share attributable to common stockholders is computed by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period. Diluted net loss attributable to common stockholders is computed by adjusting net loss attributable to common stockholders to reallocate undistributed earnings based on the potential impact of dilutive securities. Diluted net loss per share attributable to common stockholders is computed by dividing the diluted net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, including potential dilutive common shares. For purpose of this calculation, outstanding stock options, convertible preferred stock and warrants to purchase shares of convertible preferred stock are considered potential dilutive common shares.

Income Taxes—The Company accounts for income taxes using the asset and liability method. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

In evaluating the ability to recover its deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a jurisdiction-by-jurisdiction basis. In the event the Company determines that it would be able to realize its deferred income tax assets in the future in excess of their net recorded amount, it would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2020, and 2019, the Company has recorded a full valuation allowance on its deferred tax assets.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Commitments and Contingencies—Liabilities for loss contingencies arising from claims, assessments, litigation, fines, and penalties and other sources are recorded when it is probable that a liability has been incurred and the amount can be reasonably estimated. Legal costs incurred in connection with loss contingencies are expensed as incurred.

Recent Accounting Pronouncements—From time to time, new accounting pronouncements are issued by the Financial Accounting Standards Board, or FASB, or other standard setting bodies and adopted by the Company as of the specified effective date. Unless otherwise discussed, the impact of recently issued standards that are not yet effective will not have a material impact on the Company's financial position or results of operations upon adoption.

Recently Adopted Accounting Pronouncements

In June 2018, the FASB issued ASU 2018-07, *Compensation—Stock Compensation (Topic 718): Improvements to Nonemployees Share-Based Payment Accounting* ("ASU 2018-07"). ASU 2018-07 expands the scope of Topic 718 (which currently only includes share-based payments to employees) to include share-based payments issued to nonemployees for goods or services. With the adoption of ASU 2018-07, the accounting for share-based payments for non-employees and employees will be substantially the same. ASU 2018-07 is effective for fiscal years beginning after December 15, 2019, and interim periods within fiscal years beginning after December 15, 2020, with early adoption permitted. The adoption of ASU 2018-07 on January 1, 2020 did not have a material impact on the Company's financial statements and related disclosures.

In August 2018, the FASB issued ASU 2018-13, *Fair Value Measurement (Topic 820) Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement*. ASU 2018-13 resulted in certain modifications to fair value measurement disclosures, primarily related to level 3 fair value measurements. The standard was effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2019, and early adoption was permitted. The adoption of ASU 2018-13 on January 1, 2020 did not have a material impact on the Company's financial statements and related disclosures.

In December 2019, the FASB issued ASU No. 2019-12, Income Taxes (Topic 740), *Simplifying the Accounting for Income Taxes*, which is intended to simplify various aspects related to accounting for income taxes. The pronouncement is effective for fiscal years, and for interim periods within those fiscal years, beginning after December 15, 2021. ASU 2019-12 is effective for the Company beginning January 1, 2022. Early adoption is permitted. The Company has early adopted this guidance on January 1, 2020 and the impact on the Company's financial statements was not material.

In January 2020, the FASB issued ASU 2020-01, *Investments-Equity Securities (Topic 321), Investments-Equity Method and Joint Ventures (Topic 323), and Derivatives and Hedging (Topic 815).* ASU 2020-01 states any equity security transitioning from the alternative method of accounting under Topic 321 to the equity method, or vice versa, due to an observable transaction will be remeasured immediately before the transition. In addition, the ASU clarifies the accounting for certain non-derivative forward contracts or purchased call options to acquire equity securities stating such instruments will be measured using the fair value principles of Topic 321 before settlement or exercise. The ASU is effective for fiscal years beginning after December 15, 2020, and will be applied on a prospective basis. Early adoption is permitted. The Company adopted ASU 2020-01 on January 1, 2021, which did not have a material effect on the financial statements.

Recently Issued Accounting Pronouncements Not Yet Adopted

In August 2020, the FASB issued ASU 2020-06, *Debt-Debt With Conversations and Other Options (Subtopic 470-20) and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40).* The ASU simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts on an entity's own equity. Under the new ASU, convertible instruments will now more frequently accounted for as a single unit of account. That is, a conversion feature and the host instrument in which it is embedded now generally will be treated as a single unit of account unless the conversion feature requires bifurcation under Topic 815. The ASU is effective for fiscal years beginning after December 15, 2021 for public business entities, and for fiscal years beginning after December 15, 2023 for all other entities. Early adoption is permitted. The Company is in the process of evaluating the impact of this new guidance on its financial statements and related disclosures.

Correction of Errors – Subsequent to the issuance of the financial statements as of and for the year ended December 31, 2019, the Company determined that the following disclosures were incorrect, and accordingly the Company has corrected the amounts as of December 31, 2019 in the respective sections referenced as follows:

- Convertible preferred stock number of shares authorized were overstated by 5,000,000 shares from amount previously reported of 152,231,000 as disclosed on the face of the balance sheet. The Company corrected the convertible preferred stock number of shares authorized as disclosed on the face of the accompanying balance sheet as of December 31, 2019.
- Common stock number of shares issued and outstanding were overstated by 190,383 shares from amount previously reported of 16,129,938 on the face of the balance sheet. The Company corrected the common stock number of shares issued and outstanding as disclosed on the face of the accompanying balance sheet as of December 31, 2019.
- Common stock number of shares outstanding subject to repurchase were overstated by 3,001,183 shares from amount previously reported of 6,194,490 on the face of the balance sheet. The Company corrected the common stock number of shares outstanding subject to repurchase on the face of the accompanying balance sheet as of December 31, 2019.
- Options available for grant under stock plan number of shares were understated by 115,962 shares from amount previously reported of 2,990,912 in footnote 9 in the table of reserved common stock, on an as-converted basis for future issuance. The Company corrected the options available for grant number of shares as of December 31, 2019 within the referenced table in footnote 9.
- Shares available for grant Balance as of December 31, 2019 number of shares were understated by 115,962 shares from amount previously reported of 2,990,912 in footnote 10 in the table of Stock option activity under the plan. The Company corrected the shares available for issuance balance as of December 31, 2019 within the referenced table in footnote 10.
- Shares available for grant - Restricted stock repurchased for the period ended December 31, 2019 were understated by 115,963 shares from amount previously reported of 359,205 in footnote 10 in the table of Stock option activity under the plan. The Company corrected the shares available for grant-restricted stock repurchased for the period ended December 31, 2019 within the referenced table in footnote 10.
- Unvested shares related to early option exercise liability as of December 31, 2019 were overstated by 20,412 shares from amount previously reported of 3,213,719 in footnote 6 and footnote 10. The Company corrected the unvested shares as of December 31, 2019 within footnote 6 and footnote 10.

The Company believes the corrections of the disclosure errors noted above are immaterial to the previously issued financial statements as a whole.

3. FAIR VALUE MEASUREMENTS AND FAIR VALUE OF FINANCIAL INSTRUMENTS

The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1—Quoted prices in active markets for identical assets or liabilities.

Level 2—Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company’s assessment of the significance of a

particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

The Company's financial instruments consist of Level 1 assets and Level 3 liabilities. Level 1 assets are measured at fair value on a recurring basis and consist of a money market fund. Level 3 liabilities that are measured at fair value on a recurring basis consist of convertible preferred stock tranche liability.

During the periods presented, the Company has not changed the manner in which it values assets and liabilities that are measured at estimated fair value.

On a recurring basis, the Company measures certain financial assets and liabilities at fair value. The Company's fair value hierarchy for its assets and financial liabilities that are carried at fair value was as follows (in thousands):

	December 31, 2020			
	Level 1	Level 2	Level 3	Total
Cash and cash equivalents	$18,820	$ —	$ —	$18,820
Total assets	$18,820	$ —	$ —	$18,820
Liabilities—convertible preferred stock tranche liability	$ —	$ —	$ —	$ —
Total liabilities	$ —	$ —	$ —	$ —

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Cash and cash equivalents	$ 3,244	$ —	$ —	$ 3,244
Total assets	$ 3,244	$ —	$ —	$ 3,244
Liabilities—convertible preferred stock tranche liability	$ —	$ —	$ —	$ —
Total liabilities	$ —	$ —	$ —	$ —

For the year ended December 31, 2019, the Company recognized $8.7 million in realized gains on the preferred stock liability.

The changes in the carrying value of the liability were as follows:

Fair value as of December 31, 2018	$ 8,746
Recognition of convertible preferred stock tranche liability change in fair value	(8,746)
Fair value as of December 31, 2019	$ —

The fair value of the redeemable convertible preferred stock tranche liability is based on significant unobservable inputs, which represent Level 3 measurements within the fair value hierarchy. In determining the fair value of the convertible preferred stock tranche liability, the Company used the Probability-Weighted Expected Return Method, "PWERM".

There were no transfers within the hierarchy during the years ended December 31, 2020 and 2019.

4. TRANSACTIONS WITH RELATED PARTIES (AMOUNTS IN THOUSANDS)

Inception Sciences Service Agreements—Inception Sciences is wholly owned by Versant which is a majority shareholder of the Company. The Company has service agreements with Inception Sciences US, and Inception Sciences Canada whereby research and support services are provided to the Company. On June 30, 2020, the Company terminated these Inception Sciences service agreements.

Total expenses under the service agreements consist of charges for services, equipment usage, lab supplies and other out of pocket expenses as incurred. For the years ended December 31, 2020 and 2019, the Company incurred $1,315 and $4,770, respectively, in expenses under the Inception Sciences service agreements.

Related Party Notes Receivable—On November 29, 2017, three officers of the Company issued promissory notes to the Company totaling $353 related to the early exercise of their stock options which had a total exercise cost of $652. Two officers paid $298 which represents 50% of the exercise cost and the other 50% totaling $298 was recorded as notes receivable. The other officer did not pay any portion of the exercise cost and $55 was recorded as note receivable. The three notes receivable accrue interest at 2% per year and will mature on November 29, 2022. The notes receivable vest over time until maturity in conjunction with the vesting of the early-exercised stock options.

In February 2020, one of the officers left the Company and repaid $44 of which $43 was the vested portion of the note receivable and $1 was accrued interest. As of December 31, 2020 and 2019, the balance of the vested notes receivable and accrued interest was $260 and $200, respectively. For the years ended December 31, 2020 and 2019, total related party interest income was $6 and $7, respectively.

5. BALANCE SHEET ITEMS (AMOUNTS IN THOUSANDS)

Prepaid expenses and other current asset consist of the following as of December 31, 2020 and 2019 :

	2020	2019
Prepaid expenses	$ 245	$ 55
Interest receivable	—	4
Prepaid research and development costs	441	260
Notes and interest receivable	260	200
Other current assets	59	—
	$1,005	$519

Property and equipment, net, consists of the following as of December 31, 2020 and 2019:

	2020	2019
Computer equipment and software	$ 85	$ 56
Furniture and fixtures	135	126
Lab Equipment	600	583
Leasehold Improvements	746	746
Construction in process	—	6
Property and equipment	1,566	1,517
Less accumulated depreciation	(456)	(117)
Property and equipment—net	$1,110	$1,400

Depreciation expense related to property and equipment was $339 and $104 for the years ended December 31, 2020 and 2019, respectively.

Accrued liabilities as of December 31, 2020 and 2019 consists of the following:

	2020	2019
Accrued other liabilities	$441	$1,059
Accrued clinical trial liability	224	203
	$665	$1,262

As of December 31, 2020, accrued other liabilities include primarily accrual for legal services related to intellectual properties, debt issuance and corporate legal, and research and development activities totaling $352. As of December 31, 2019, accrued other liabilities include primarily accrual for legal services related to intellectual properties and preferred stock issuance, and research and development activities totaling $271.

6. EARLY OPTION EXERCISE LIABILITY (AMOUNTS IN THOUSANDS)

The recorded amount of the early option exercise liability relates to restricted stock awards and stock options granted to certain employees and contractors that were early-exercised before they became vested. The early option exercise liability decreases as the restricted stock awards and stock options vest over time or if the Company decides to repurchase them, and the amount of decrease is recorded in common stock and additional paid-in capital. During 2020, certain early-exercised unvested stock options of 32,635 were repurchased by the Company for $1. As of December 31, 2020 and 2019, the early option exercise liability was $79 and $241, respectively, which represents unvested shares of 900,509 and 3,193,307. The unvested shares purchased by the employees are not deemed, for accounting purposes, to be issued and outstanding.

7. COMMITMENTS AND CONTINGENCIES (AMOUNTS IN THOUSANDS)

Facility Lease Agreement—In February 2019, the Company entered into a 5-year office lease agreement for a 9,780 square feet facility in South San Francisco, California. The remaining lease term of the office lease is three years and two months as of December 31, 2020, and the discount rate used to calculate the Company's right of use asset and lease liability is 4.25%. There are no other leases as of December 31, 2020 and 2019.

As of December 31, 2020 and 2019, the balance of the operating lease right of use assets were $1,877 and $2,353, respectively, and the related operating lease liability were $2,439 and $2,364, respectively, as shown in the accompanying balance sheets.

Related to the facility lease agreement, the Company entered into a letter of credit with a bank to deposit $51 as security rent deposit for the South San Francisco office. This amount is shown as other noncurrent assets in the accompanying balance sheets as of December 31, 2020 and 2019.

Rent expense was $665 for the year ended December 31, 2020 and $623 for the year ended December 31, 2019.

In 2020 and 2019 the Company paid a total of $734 and $529, respectively for the operating lease liability.

Future minimum annual lease payments under the Company's operating lease liabilities as of December 31, 2020 is as follows:

Year Ending	Total Commitment
2021	$ 801
2022	821
2023	841
2024	141
2025	—
Total minimum lease payments	2,604
Less: imputed interest	(165)
Present value of operating lease obligations	2,439
Less: current portion	(712)
Noncurrent operating lease obligations	$ 1,727

Guarantees and Indemnifications—In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2020, and 2019, the Company does not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

Legal Proceedings – From time to time, the Company may become involved in litigation relating to claims arising from the ordinary course of business. Management believes that there are no actions pending against the Company currently, the ultimate disposition of which would have a material adverse effect on the Company's results of operations, financial condition or cash flows.

8. CONVERTIBLE PREFERRED STOCK

As of December 31, 2020, the Company was authorized to issue up to 135,936,731 shares of preferred stock at a par value of $0.001.

The authorized, issued and outstanding shares of the convertible preferred stock and liquidation preferences at December 31, 2020 and 2019 were as follows (in thousands except share and per share amounts):

December 31, 2020

Series	Shares Authorized	Shares Issued and Outstanding	Per Share Liquidation Preference	Aggregate Liquidation Amount	Proceeds Net of Issuance Cost	Net Carrying Value
Series A	17,000,000	17,000,000	$ 1.00	$ 17,000	$ 16,982	$ 16,982
Series B	25,186,738	25,186,738	1.00	25,187	24,943	12,235
Series B-1	93,749,993	72,499,993	0.80	58,000	57,489	57,489
	135,936,731	114,686,731		$ 100,187	$ 99,414	$ 86,706

December 31, 2019

Series	Shares Authorized	Shares Issued and Outstanding	Per Share Liquidation Preference	Aggregate Liquidation Amount	Proceeds Net of Issuance Cost	Net Carrying Value
Series A	17,000,000	17,000,000	$ 1.00	$ 17,000	$ 16,982	$ 16,982
Series B	72,293,000	25,186,738	1.00	25,187	24,943	12,235
Series B-1	57,938,000	28,749,997	0.80	23,000	22,755	22,755
	147,231,000	70,936,735		$ 65,187	$ 64,680	$ 51,972

In October 2011, the Company received a commitment from its venture investor for a Series A Preferred Stock financing totaling $10 million to be taken down in two tranches of $5 million each. Upon execution of the stock purchase agreement, the Company received the first tranche of $5 million, which included $2,399 in cash proceeds and the conversion of notes payable and accrued interest totaling $2,601 for issuing 5,000,000 shares of its Series A Preferred Stock. In June 2012, the Company received cash proceeds of $5 million related to the second tranche of the Series A Preferred Stock financing from the issuance of 5,000,000 shares of Series A Preferred Stock.

In August 2015, the Company issued an additional 2,000,000 shares of Series A Preferred Stock to its venture investor for cash proceeds of $2 million.

In September 2016, the Company issued an additional 5,000,000 shares of Series A Preferred Stock to its venture investor for cash proceeds of $5 million.

In February 2018, the Company issued 25,186,738 shares of Series B Preferred Stock for $1.00 per share in connection with the closing of the Series B Preferred Stock Purchase Agreement. The Company's convertible notes of $8.0 million and accrued interest was converted as part of the Series B offering. Investors in the Series B convertible preferred stock financing also received freestanding rights to purchase additional shares of Series B convertible preferred stock on the same terms as the first closing upon completion of certain defined milestones or waiver of the milestones by the holders of at least 67% of the outstanding convertible preferred stock, voting as a single class on an as converted basis. In August 2018, the terms of the Series B Agreement were amended. The amendment allowed for the purchase of Series B-1 shares at a price of $0.80 per share based upon the completion of certain amended milestones. These milestones are as follows:

Second Tranche Milestones:

- Clearance by the U.S. Food and Drug Administration of the filing by the Company of an investigational new drug application (IND) for PPARα antagonist.
- Selection of an EP2/EP4 dual antagonist DC.

Third Tranche Milestones:

- Demonstration of safety/tolerability and clinical Proof of Mechanism with PPARα antagonist.
- Single additional program having a data package that is sufficient for submitting an IND.

The investors' rights to purchase Series B and B-1 convertible preferred stock represent a freestanding financial instrument accounted for as a liability measured at fair value at inception and remeasured at fair value each reporting date. Based on the probability vs. 100% of the milestones for the purchase of Series B-1 shares as of December 31, 2019, this resulted in a fair value of $0 at such date. Changes in fair value are recognized in the statement of operations. The proceeds from the initial closing of the Series B convertible preferred stock of $25.2 million were allocated to the convertible preferred stock tranche liability at its initial fair value of $12.7 million with the remaining amount allocated to the carrying value of the Series B convertible preferred stock. The fair value of the convertible preferred stock tranche liability was determined using an option pricing model approach.

In February 2019, the Company issued 28,749,997 shares of Series B-1 preferred stock for $0.80 per share for total cash proceeds of $23 million.

In January 2020, the Company issued 43,749,996 shares of Series B-1 preferred stock for $0.80 per share for total cash proceeds of $35 million.

The significant rights, preferences, and privileges of the convertible preferred stock as of December 31, 2020 were as follows:

Dividends—The holders of the Company's convertible preferred stock are entitled to receive noncumulative dividends of 8% per share (as adjusted for stock splits, combinations, and reorganizations) per annum on each outstanding share of Series convertible preferred stock. Such dividends shall be payable only when and if declared by the Board of Directors. As of December 31, 2020, and 2019, the Company's Board of Directors had not declared any dividends. Dividends on convertible preferred stock shall be payable in preference to and prior to any payments of any dividends on common stock. No dividends have been declared to date.

Conversion—The Company's preferred stock is convertible, at the option of the holder into an equal number of shares of common stock, at the option of the holder, subject to certain anti-dilution adjustments.

Each share of preferred stock is automatically converted into common stock immediately upon (i) the Company's sale of its common stock in a firm commitment underwritten public offering pursuant to a registration statement under the Securities Act of 1933, as amended, in which per share price is at least $3.00 (as adjusted), and the gross cash proceeds are at least $50 million or (ii) the affirmative vote of the requisite preferred holders.

The conversion of Series B shares, either at the option of the holder or automatically, requires the prior vote or consent of the holders of at least 70% of the Series B preferred stock.

Voting Rights—The holders of preferred stock are entitled to one vote for each share of common stock into which such preferred stock could then be converted; and with respect to such vote, such holder shall have full voting rights and powers equal to the voting rights and powers of the holders of common stock.

Liquidation—The holders of preferred stock are entitled to receive liquidation preferences at an amount per share of preferred stock equal to the original price plus all declared and unpaid dividends on the preferred stock. Liquidation payments to the holders of preferred stock have priority and are made in preference to any payments to the holders of common stock. After full payment of the liquidation preference to the holders of the preferred stock, the remaining assets, if any, will be distributed ratably to the holders of the common stock and preferred stock on an as-if-converted to common stock basis.

Redemption and Balance Sheet Classification— The convertible preferred stock is recorded within mezzanine equity because while it is not mandatorily redeemable, it will become redeemable at the option of the stockholders upon the occurrence of certain deemed liquidation events that are considered not solely within the Company's control.

9. COMMON STOCK

As of December 31, 2020, the Company was authorized to issue 196,000,000 shares of common stock at a par value of $0.001. Of the 196,000,000 common stock shares authorized, 16,374,711 are legally issued and outstanding at December 31, 2020, with 900,509 shares subject to repurchase due to remaining vesting requirements. Common stockholders are entitled to dividends as declared by the Board of Directors, subject to rights of holders of all classes of stock outstanding having priority rights as to dividends. There have been no dividends declared to date. The holders of each share of common stock are entitled to one vote. Except for effecting or validating certain specific actions intended to protect the preferred stockholders, the holders of common stock vote together with preferred stockholders and have the right to elect one member of the Company's Board of Directors.

The fair value of the shares of common stock has historically been determined by management and approved by the Board of Directors. Because there has been no public market for the Company's common stock, the Board of Directors has determined the fair value of the common stock by considering a number of objective and subjective factors, including contemporaneous valuations performed by an unrelated third-party specialist, important developments in the Company's operations, the prices at which the Company sold shares of convertible preferred common stock, the rights, privileges, and preferences of the Company's convertible preferred stock relative to the Company's common stock, valuations of comparable public companies, operating and financial performance, the lack of liquidity of capital stock, and general and industry-specific economic outlook. Valuations performed by the third-party valuation specialist used the methodologies, approaches, and assumptions consistent with the American Institute of Certified Public Accountants Accounting and Valuation Guide, Valuation of Privately-Held-Company Equity Securities Issued as Compensation (AICPA Accounting and Valuation Guide).

The Company had reserved common stock, on an as-converted basis for future issuance as follows:

	2020	2019
Conversion of Series A Preferred Stock	17,000,000	17,000,000
Conversion of Series B Preferred Stock	25,186,738	25,186,738
Conversion of Series B-1 Preferred Stock	72,499,993	28,749,997
Options available for grant under stock plan	15,211,101	3,106,874
Issuance of common stock upon exercise of stock options under stock plan	14,042,429	8,227,470
	143,940,261	82,271,079

10. STOCK COMPENSATION

In 2011 the Company adopted the 2011 Equity Incentive Plan, and in 2017, the Company adopted the 2017 Equity Incentive Plan, together "the Plans". Upon adoption of the 2017 Equity Incentive Plan, the 2011 Equity Incentive Plan was terminated. Both the Plans provide for the granting of stock awards to employees, directors and consultants of the Company. Awards issuable under the Plans include incentive stock options (ISO), nonqualified stock options (NSO), stock appreciation rights (SAR), restricted stock awards, restricted stock unit awards and other stock awards.

Options to purchase the Company's common stock may be granted at a price not less than the fair market value in the case of both NSOs and ISOs, except for an employee or non-employee with options who owns more than 10 percent of the voting power of all classes of stock of the Company, in which case the exercise price shall be no less than 110 percent of the fair market value per share on the grant date. Stock options granted under the Plans generally vest over four years and expire no later than ten (10) years from the date of grant. Vested options can be exercised at any time.

The grant date fair market value of the shares of common stock underlying stock options has historically been determined by the Company's Board of Directors. Because there has been no public market for the Company's common stock, the Board of Directors exercises reasonable judgment and considers a number of objective and subjective factors to determine the best estimate of the fair market value, which include valuations performed by an independent third-party, important developments in the Company's operations, sales of convertible preferred stock, actual operating results, financial performance, the conditions in the life sciences industry, the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of the Company's common stock.

Stock option activity under the Plan is set forth below:

	Shares Available for Grant	Total Options Outstanding	Weighted-Average Exercise Price
Balance—January 1, 2019	4,959,573	6,190,013	$ 0.15
Additional shares authorized	—	—	—
Restricted stock repurchased	475,168	—	—
Granted	(5,049,563)	5,049,563	0.16
Exercised	—	(290,410)	0.15
Cancelled and forfeited	2,721,696	(2,721,696)	0.15
Balance—December 31, 2019	3,106,874	8,227,470	0.16
Additional shares authorized	18,366,565	—	—
Granted	(6,971,754)	6,971,754	0.19
Exercised	—	(447,379)	0.15
Cancelled and forfeited	709,416	(709,416)	0.16
Balance—December 31, 2020	15,211,101	14,042,429	0.17

The following table summarizes information about stock options outstanding at December 31, 2020:

	Shares	Weighted Average Remaining Contractual Life (In Years)	Weighted Average Exercise Price	Aggregate Intrinsic Value
Options outstanding	14,042,429	8.67	$ 0.17	$ 2,214,774
Vested and expected to vest	12,911,246	8.75	$ 0.17	$ 2,022,623
Exercisable	3,805,570	7.78	$ 0.16	$ 646,883

The intrinsic value of options exercised during 2020 and 2019 was $16,408 and zero, respectively, and is calculated based on the difference between the exercise price and the fair value of the Company common stock as of the exercise date.

Employee Stock Options—During the years ended December 31, 2020 and 2019, the Company granted stock options to employees to purchase 6,524,854 and 4,722,063, shares of common stock with a weighted-average grant date fair value of $0.11 and $0.09 per share, respectively.

As of December 31, 2020, there was total unrecognized compensation costs related to unvested employee stock options of $942. These costs are expected to be recognized over a weighted-average period of approximately 1.6 years.

The Company estimated the fair value of stock options using the Black-Scholes option pricing valuation model. The fair value of employee stock options is being amortized on the straight-line basis over the requisite service period of the awards. The fair value of employee stock options was estimated using the following range of assumptions during 2020:

Expected term (in years)	6.0–6.1
Expected volatility	62%–66%
Risk-free interest rate	0.4%–0.5%
Dividends	0%

Expected Term—The expected term of options granted represents the period of time that the options are expected to be outstanding. Due to the lack of historical exercise history, the expected term of the

Company's employee stock options has been determined utilizing the simplified method for awards that qualify as plain-vanilla options.

Expected Volatility—The expected stock price volatility assumption was determined by examining the historical volatilities for industry peers, as the Company did not have any trading history for the Company's common stock. The Company will continue to analyze the historical stock price volatility and expected term assumption as more historical data for the Company's common stock becomes available.

Risk-Free Interest Rate—The risk-free interest rate assumption is based on the U.S. Treasury instruments whose term was consistent with the expected term of the Company's stock options.

Dividends—The Company has not paid any cash dividends on common stock since inception and does not anticipate paying any dividends in the foreseeable future. Consequently, an expected dividend yield of zero was used.

Non-Employee Stock Options—During the years ended December 31, 2020 and 2019, the Company granted stock options to non-employees to purchase 446,900 and 327,500 shares of common stock, respectively. During 2019 the fair value of stock options granted to non-employees was calculated at each vesting date. Upon the Company's adoption of ASU No. 2018-07 all unvested shares were valued as of January 1, 2020 and all subsequent options were valued at the grant date.

As of December 31, 2020, there was total unrecognized compensation costs related to unvested non-employee stock options of $33. These costs are expected to be recognized over a weighted-average period of approximately 0.7 years.

The Company estimated the fair value of stock options using the Black-Scholes option pricing valuation model. The fair value of non-employee stock options is being amortized on the straight-line basis over the requisite service period of the awards. The fair value of non-employee stock options was estimated using the following range of assumptions during 2020:

Expected term (in years)	10
Expected volatility	64%–65%
Risk-free interest rate	0.70%
Dividends	0%

Expected Term—The expected term of options granted represents the period of time that the options are expected to be outstanding. The Company has valued its non-employee stock options using the contractual term as the expected term.

Expected Volatility—The expected stock price volatility assumption was determined by examining the historical volatilities for industry peers, as the Company did not have any trading history for the Company's common stock. The Company will continue to analyze the historical stock price volatility and expected term assumption as more historical data for the Company's common stock becomes available.

Risk-Free Interest Rate—The risk-free interest rate assumption is based on the U.S. Treasury instruments whose term was consistent with the expected term of the Company's stock options.

Dividends—The Company has not paid any cash dividends on common stock since inception and does not anticipate paying any dividends in the foreseeable future. Consequently, an expected dividend yield of zero was used.

Restricted Stock—In 2011 the Company sold 2,440,000 shares of common stock to founders at $0.001 per share, that were subject to certain vesting restrictions. During 2017 the Company modified the vesting schedules of 1,406,673 of these shares, 666,667 of which affected one employee and 740,006 affected 21 non-employees. The modifications provided for a four-year vesting schedule for shares that were not previously expected to vest. The modifications were accounted for as cancellations and re-issuance of shares.

The shares to employees and non-employees are valued based on an estimate of the Company's common stock price on the grant date.

The activity of the unvested restricted stock during 2020 and 2019 is as follows:

Unvested balance—January 1, 2019	853,551
Vested	(288,057)
Repurchased	(79,309)
Unvested balance—December 31, 2019	486,185
Vested	(486,185)
Unvested balance—December 31, 2020	0

All stock-based compensation related to restricted stock has been recognized as of December 31, 2020.

Stock-Based Compensation Expense—The following table summarizes the components of stock-based compensation expense recognized in the Company's statement of operations during 2020 and 2019:

Share Based Compensation	2020	2019
Research and development	$ 389	$ 191
General and administrative	64	119
	$ 453	$ 310

Early Exercise Liability—Stock options may be exercised, and restricted stock may be purchased prior to the time that the awards have vested, provided that such shares shall remain subject to repurchase until such time as they have vested. The right to repurchase these shares generally lapses over three to four years. As of December 31, 2020 and 2019, there were 900,509 and 3,193,307 unvested shares representing an early exercise liability of $79 and $241, respectively. The unvested shares purchased by the employees are not deemed, for accounting purposes, to be issued and outstanding.

11. RETIREMENT PLAN

The Company participates in a qualified 401(k) Plan sponsored by its professional service organization. The retirement plan is a defined contribution plan covering eligible employees. Participants may contribute a portion of their annual compensation limited to a maximum annual amount set by the Internal Revenue Service. There was no contribution from the Company in 2020 and 2019.

12. TAXES

The Company has no provision for income taxes in 2020. This differs from the amounts computed by applying the statutory income tax rate of 21% to pre-tax loss primarily due to research credits generated and changes in the valuation allowance.

The provision (benefit) for income taxes consists of the following (in thousands):

	Year Ended December 31,	
	2020	2019
Current:		
Federal	$ —	$ —
State	—	1
Total Current	—	1

	Year Ended December 31,	
	2020	2019
Deferred:		
Federal	$ —	$ —
State	—	—
Total Deferred	—	—
	$ —	
Provision (Benefit) for income taxes		**$ 1**

Income tax provision (benefit) related to continuing operations differ from the amounts computed by applying the statutory income tax rate of 21% to pretax loss as follows:

	Year Ended December 31,	
U.S. Federal provision (benefit)	2020	2019
At statutory rate	$ (4,033)	$ (3,017)
State taxes	—	1
Valuation allowance	4,596	5,380
Tax credits	(604)	(580)
Stock based compensation	37	19
Permanent differences	4	34
Mark-to-market adjustments	—	(1,836)
Total	**$ —**	**$ 1**

Significant components of the Company's deferred tax assets at December 31, 2020 and 2019 are shown below.

	Year Ended December 31,	
	2020	2019
Deferred tax assets:		
Net operating losses	$ 23,943	$ 18,657
Research and development tax credits	4,597	3,778
Amortization	78	93
Lease liability	714	705
Other	458	323
Total gross deferred tax assets	29,790	23,556
Less: valuation allowance	(29,073)	(22,677)
Total deferred tax assets	717	879
Deferred tax liabilities:		
Right of use assets	(550)	(702)
Fixed assets	(167)	(177)
Total gross deferred tax liabilities	(717)	(879)
Net deferred tax assets	$ —	$ —

The Company has recorded a full valuation allowance against its net deferred tax assets due to the uncertainty as to whether such assets will be realized. The valuation allowance increased by $6.4 million from December 31, 2019 to December 31, 2020 due primarily to the generation of net operating losses and research and development credits.

As of December 31, 2020, the Company has net operating loss carryforwards for federal and California income tax purposes of approximately $80.9 million and $80.3 million, respectively. As of December 31, 2019, the Company has net operating loss carryforwards for federal and California income tax purposes of approximately $62.9 million and $63.3 million, respectively.

The federal and state net operating loss carryforwards begin to expire in 2031, if not utilized. Federal net operating losses of $40.0 million are not subject to expiration.

As of December 31, 2020, the Company also has federal and state research and development carryforwards of approximately $3.9 million and $1.9 million, respectively. As of December 31, 2019, the Company also has federal and state research and development carryforwards of approximately $3.1 million and $1.6 million, respectively. The federal credits begin to expire in 2031 and the state credits can be carried forward indefinitely.

Utilization of some of the federal and state net operating loss and credit carryforwards may be subject to annual limitations due to the “change in ownership” provisions of the Internal Revenue Code of 1986 and similar state provisions. The annual limitations may result in the expiration of net operating losses and credits before utilization. The Company has not performed a Section 382 study as of December 31, 2020. State net operating losses are being computed based on an alternate apportionment methodology. Amounts reported can change accordingly.

As of December 31, 2020, the Company has approximately $1.3 million in unrecognized tax benefits, excluding indirect tax effects. Of the total unrecognized tax benefits at December 31, 2020, $1.3 million was recorded as a reduction to deferred tax assets, which caused a corresponding reduction in the Company’s valuation allowance of $1.3 million. The Company does not anticipate that the amount of unrecognized tax benefits as of December 31, 2020 will change materially within the 12-month period following December 31, 2020.

The Company has the following activity relating to unrecognized tax benefits:

	Year Ended December 31,	
	2020	2019
Beginning balance	1,080	860
Gross increase - tax positions in prior periods	—	—
Gross decreases - tax positions in prior periods	—	(44)
Gross increases - tax position in current period	200	264
Settlements	—	—
Lapses in statutes of limitations	—	—
Ending balance	1,280	1,080

The Company’s practice is to recognize interest and/or penalties related to income tax matters in income tax expense. The Company had no accrual for interest and penalties on the accompanying balance sheet as of December 31, 2020 and has not recognized penalties and/or interest in the accompanying statement of operations for the year ended December 31, 2020.

The Company is subject to taxation in the United States and various states. The Company's tax years from inception are subject to examination by the IRS and state tax authorities due to the carryforward of unutilized net operating losses and research and development credits.

13. NET LOSS PER SHARE

The following table sets forth the computation of the Company's basis in diluted net loss per share for the years ended December 31, 2020 and 2019 (in thousands except share and per share amounts):

	Year Ended December 31,	
	2020	2019
Numerator:		
Net loss	$ (19,208)	$ (14,365)
Denominator:		
Weighted-average common shares outstanding	16,184,669	15,924,843
Less: Weighted-average unvested restricted shares and shares subject to repurchase	(1,645,491)	(3,346,636)
Weighted-average shares used to computing basic and diluted net loss per share	14,539,178	12,578,207
Net loss per share attributable to common stockholders - basic and diluted	**$ (1.32)**	**$ (1.14)**

As of December 31, 2020 and 2019, the Company's potentially dilutive securities included preferred stock, unvested restricted stock and stock options, which have been excluded from the computation of diluted net loss per share attributable to common stockholders as the effect would be anti-dilutive. Based on the amounts outstanding as of December 31, 2020 and 2019, the Company excluded the following potential common shares from the computation of diluted net loss per share attributable to common stockholders because including them would have had an anti-dilutive effect:

	As of December 31,	
	2020	2019
Series A Preferred Stock	17,000,000	17,000,000
Series B Preferred Stock	25,186,738	25,186,738
Series B-1 Preferred Stock	72,499,993	28,749,997
Options to purchase common stock	14,042,429	8,227,470
Unvested restricted common stock	900,509	3,193,307
	129,629,669	82,357,512

14. SUBSEQUENT EVENTS

The Company has evaluated subsequent events occurring through May 10, 2021, the date when these financial statements are available to be issued.

Term Loan—On January 15, 2021, the Company entered into a loan agreement with a lender to borrow a term loan amount of $35.0 million to be funded in three tranches. Tranche A of $15.0 million was wired to the Company on January 15, 2021. Tranche B of $10.0 million will be available through March 31, 2022 contingent upon achievement of each of the following: i) receipt of at least $50,000,000 in Series C equity capital, ii) initiation of the Phase 1 combination study of TPST-1495 or monotherapy expansion study, and iii) initiation of Phase 2 trial of TPST-1120 or the 1L Triplet Collaboration study. And Tranche C of $10.0 million is available at lender's option. The term loan matures on August 1, 2025 and has an annual floating interest rate of 7.15% which is an Index Rate plus 7%. Index Rate is the greater of (i) 30-day US LIBOR or (ii) 0.15%. Concurrent with the funding of an amount under each Tranche, the Company will

grant the lender a warrant to purchase shares of Series B-1 preferred stock equal to 1% of the funded amount. For Tranche A, the Company issued 187,500 Series B-1 stock warrants. No Series B-1 preferred stock warrants have been issued for Trances B and C since those tranches have not been funded yet.

Reverse Merger—On March 29, 2021, Tempest entered into an Agreement and Plan of Merger (the "Merger Agreement") with Millendo Therapeutics, Inc., or ("Millendo"), pursuant to which, among other things, subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, a wholly owned subsidiary of Millendo will merge with and into Tempest, with Tempest becoming a wholly-owned subsidiary of Millendo and the surviving corporation of the merger. At the closing of the merger, each outstanding share of Tempest's capital stock (including preferred stock) will be converted into the right to receive shares of common stock of Millendo at a ratio whereby the equity holders of Tempest will become the majority owners (81.5%) of Millendo's outstanding common stock on a full-diluted basis upon the close of the merger (the "Merger").

The Merger will be accounted for as a reverse recapitalization in accordance with U.S. GAAP. Under this method of accounting, Tempest will be deemed to be the accounting acquirer for financial reporting purposes. This determination was primarily based on the expectations that, immediately following the Merger: (1) Tempest stockholders will own substantial majority of the voting rights; (2) Tempest will designate a majority of the initial members of the board of directors of the combined organization; and (3) Tempest's senior management will hold key positions in senior management of the combined organization. Accordingly, for accounting purposes, the Merger will be treated as the equivalent of Tempest issuing stock to acquire the net assets of Millendo. As a result of the Merger, the net assets of Millendo will be recorded at their acquisition-date fair value in the financial statements of Tempest and the reported operating results prior to the Merger will be those of Tempest. Any excess in consideration paid will be presented as cost of equity.

Concurrent with the execution and delivery of the Merger Agreement, Tempest entered into Funding Agreements with certain investors named therein, pursuant to which the investors agreed to purchase, in the aggregate, $30.0 million of Tempest common stock convertible into securities of Millendo.

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UNAUDITED PRO FORMA CONDENSED COMBINED FINANCIAL INFORMATION

On March 29, 2021, Millendo Therapeutics, Inc., a Delaware corporation ("Millendo"), Tempest Therapeutics, Inc., a Delaware corporation ("Tempest"), and Mars Merger Sub, a Delaware corporation and a wholly-owned subsidiary of Millendo ("Merger Sub") entered into an agreement and plan of merger (the "Merger Agreement"). Upon the terms and subject to the satisfaction or waiver of the conditions set forth in the Merger Agreement, including approval of the transaction by Millendo's stockholders and Tempest's stockholders, Merger Sub will merge with and into Tempest, with Tempest becoming a wholly-owned subsidiary of Millendo and the surviving corporation of the merger (the "Merger"). At the effective time of the Merger, or the Effective Time, Millendo will change its name to Tempest Therapeutics, Inc. ("Public Tempest").

At the effective time of the Merger ("Effective Time"), each share of Tempest's common stock outstanding immediately prior to the Effective Time, including shares of Tempest's common stock that are issued pursuant to the Pre-Closing Financing will be converted into the right to receive a number of shares of Millendo's common stock based on agreed upon ratio by the parties ("the Exchange Ratio"). The Exchange Ratio was initially estimated to be 0.488 shares of Millendo's common stock for each share of Tempest's common stock, and is subject to change to account for, among other things, Millendo's net cash as of the business day prior to the closing (the "Closing") of the Merger. The Exchange Ratio also does not give effect to the proposed Millendo Reverse Stock Split (as defined below) because the proposed reverse stock split is a range and is not final. Each share of Tempest's convertible preferred stock outstanding immediately prior to the Effective Time is expected to be converted into shares of Tempest's common stock in accordance with its terms, which would then convert into the right to receive shares of Millendo's common stock along with all other shares of Tempest's common stock as described above. Under the Exchange Ratio formula in the Merger Agreement, the former Tempest equity holders immediately before the Effective Time are expected to own approximately 81.5% of the outstanding capital stock of Millendo on a fully-diluted basis, and the stockholders of Millendo immediately before the Effective Time are expected to own approximately 18.5% of the outstanding capital stock of Millendo on a fully-diluted basis, subject to adjustment based upon whether Millendo's net cash at the closing of the Merger is greater than $18.7 million or less than $15.3 million and other potential adjustments.

A reverse stock split of Millendo's common stock will be effectuated prior to the Closing at a ratio of between 1 to 10 and 1 to 15 ("Millendo Reverse Stock Split")

Because, among other things, the number of shares of Millendo's common stock issuable to Tempest's securityholders is determined based on Millendo's net cash balance on the business day prior to the Closing and the capitalization of Tempest and Millendo at the Closing, Millendo's securityholders cannot be certain of the exact number of shares that will be issued to (or reserved for issuance to) Tempest's securityholders when Millendo's stockholders vote on the proposals. The Exchange Ratio referenced above is an estimate only and the final Exchange Ratio will be determined pursuant to a formula described in more detail in the Merger Agreement and in this proxy statement/prospectus.

Concurrently with the execution and delivery of the Merger Agreement, certain parties have entered into agreements with Tempest, pursuant to which they have agreed, subject to terms and conditions of such agreements, to purchase prior to the consummation of the Merger shares of Tempest common stock for an aggregate purchase price of approximately $28.1 million, net of issuance costs of $1.9 million.

The following unaudited pro forma condensed combined financial information gives effect to the (i) Merger and (ii) the Pre-Closing Financing, but does not give effect to the proposed Millendo Reverse Stock Split because the proposed reverse stock split is a range and is not final.

In the unaudited pro forma combined financial statements, the Merger has been accounted for as a reverse recapitalization under U.S. GAAP because the assets of Millendo at the Effective Date are expected to be primarily cash and non-operating assets. Tempest was determined to be the accounting acquirer based upon the

terms of the Merger and other factors including: (1) Tempest stockholders will own a substantial majority of the voting rights of the combined company; (2) Tempest will designate a majority (six of seven) of the initial members of the board of directors of the combined company; and (3) Tempest's senior management will hold all key positions in senior management of the combined company.

As a result of Tempest being treated as the accounting acquirer, Tempest's assets and liabilities will be recorded at their precombination carrying amounts and the historical operations that are reflected in the unaudited pro forma condensed combined financial information will be those of Tempest. Millendo's assets and liabilities will be measured and recognized at their fair values as of the effective date of the Merger, and combined with the assets, liabilities, and results of operations of Tempest after the consummation of the Merger. As a result, upon consummation of the Merger, the historical financial statements of Tempest will become the historical consolidated financial statements of the combined company.

The unaudited pro forma combined balance sheet data as of December 31, 2020 assumes that the Merger took place on December 31, 2020 and combines the Millendo and Tempest historical balance sheets as of December 31, 2020. The unaudited pro forma condensed combined statements of operations assumes that the Merger took place on January 1, 2020 and combines the historical results of Millendo and Tempest for the year ended December 31, 2020.

The historical financial statements of Millendo and Tempest have been adjusted to give pro forma effect to reflect the accounting for the transaction in accordance with U.S. GAAP. The adjustments presented on the unaudited pro forma condensed combined financial statements have been identified and presented to provide relevant information necessary for an accurate understanding of the combined company upon consummation of the Merger.

The unaudited pro forma condensed combined financial information is based on assumptions and adjustments that are described in the accompanying notes. The unaudited pro forma condensed combined financial information is for illustrative purposes only. The financial results may have been different had the companies always been combined. The unaudited pro forma condensed combined financial information should not be relied upon as being indicative of the historical results that would have been achieved had the companies always been combined or the future results that the combined company will experience. The actual amounts recorded as of the completion of the Merger may differ materially from the information presented in these unaudited pro forma combined financial information as a result, if any, of the amount of capital raised by Tempest between the signing of the Merger Agreement and Closing, the amount of cash used by Millendo's operations between the signing of the Merger Agreement and the Closing, the timing of Closing of the Merger, and other changes in Millendo's assets and liabilities that occur prior to the completion of the Merger.

The unaudited pro forma condensed combined financial statements, including the notes thereto, should be read in conjunction with the separate historical consolidated financial statements of Millendo and Tempest and the sections of this proxy statement/prospectus titled "*Millendo Management's Discussion and Analysis of Financial Condition and Results of Operations*" and "*Tempest Management's Discussion and Analysis of Financial Condition and Results of Operations*." Both Millendo's historical audited consolidated financial statements for the year ended December 31, 2020 and Tempest's historical audited financial statements for the year ended December 31, 2020 appear elsewhere in this proxy statement/prospectus.

Unaudited Pro Forma Condensed Combined Balance Sheet
As of December 31, 2020
(in thousands, except share and per share data)

	Tempest	Millendo	Transaction Accounting Adjustments	Note 4	Pro Forma Combined Total
ASSETS					
Current assets:					
Cash and cash equivalents	$ 18,820	$ 38,174	$ 28,050	A	$ 85,044
Restricted cash	—	484	—		484
Prepaid expenses and other current assets	1,005	1,929	—		2,934
Refundable tax credit	—	314	—		314
Total current assets	19,825	40,901	28,050		88,776
Operating lease right-of-use assets	1,877	2,157	215	**E**	4,249
Property and equipment, net	1,110	275	—		1,385
Other non-current assets	51	76	—		127
Total assets	$ 22,863	$ 43,409	$ 28,265		$ 94,537
LIABILITIES, CONVERTIBLE PREFERRED STOCK & STOCKHOLDERS' EQUITY (DEFICIT)					
Current liabilities:					
Accounts payable	$ 1,071	$ 1,486	$ —		$ 2,557
Accrued liabilities	665	3,547	11,012	B, C, D	15,224
Current portion of operating lease liabilities	712	737	—		1,449
Accrued compensation	695	1,978	—		2,673
Current portion of debt	—	239	—		239
Early option exercise liability	79	—	—		79
Total current liabilities	3,222	7,987	11,012		22,221
Operating lease liabilities, net of current portion	1,727	1,635	—		3,362
Debt, net of current portion	—	61	—		61
Total liabilities	4,949	9,683	11,012		25,644
Stockholders' equity (deficit):					—
Convertible preferred stock	86,707	—	(86,707)	**F**	—
Common stock	15	19	65	**G**	99
Additional paid-in capital	2,953	277,647	(132,744)	G	147,856
Accumulated deficit	(71,761)	(245,060)	237,091	G	(79,730)
Accumulated other comprehensive income	—	452	(452)	G	—
Total stockholders' equity (deficit)	(68,793)	33,058	103,960		68,225
Equity attributable to noncontrolling interests	—	668	—		668
Total stockholders' equity (deficit)	(68,793)	33,726	103,960		68,893
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	$ 22,863	$ 43,409	$ 28,265		$ 94,537

Unaudited Pro Forma Condensed Combined Statements of Operations
Year Ended December 31, 2020
(in thousands, except share and per share data)

	Tempest	Millendo	Transaction Accounting Adjustments	Note 4	Pro Forma Combined
Operating expenses:					
Research and development	$ 14,389	$ 20,374	—		$ 34,763
General and administrative	4,909	15,598	7,969	**H, I, J**	28,476
Total operating expenses	19,298	35,972	7,969		63,239
Loss from operations	(19,298)	(35,972)	(7,969)		(63,239)
Other income (expense):			—		
Interest income	90	155	—		245
Other expense	—	(589)	—		(589)
Total other income (expense)	90	(434)	—		(344)
Net loss	$ (19,208)	$ (36,406)	$ (7,969)		$ (63,583)
Weighted average common stock outstanding —basic and diluted	14,539,178	18,862,537	—	**K**	97,902,613
Net loss per share attributable to common stockholders—basic and diluted	$ (1.32)	$ (1.93)	—		$ (0.65)

Notes to Unaudited Pro Forma Combined Financial Statements

1. Description of the Transactions

Merger

On March 29, 2021, Millendo, Tempest and Merger Sub entered into the Merger Agreement. At the Effective Time of the Merger, each share of Tempest common stock outstanding immediately prior to the Effective Time, including shares of Tempest's convertible preferred stock that is expected to be converted into common stock as described above, will be converted into the right to receive a number of shares of Millendo's common stock equal to the Exchange Ratio. The Exchange Ratio is initially estimated to be 0.488 of Millendo's Common Stock for each share of Tempest's Common Stock. Under the Exchange Ratio formula in the Merger Agreement, the former Tempest equity holders immediately before the Effective Time are expected to own approximately 81.5% of the outstanding capital stock of Millendo on a fully-diluted basis, and the stockholders of Millendo immediately before the Effective Time are expected to own approximately 18.5% of the outstanding capital stock of Millendo on a fully-diluted basis, subject to adjustment based upon whether Millendo's net cash at the closing of the Merger is greater than $18.7 million or less than $15.3 million and other potential adjustments.

Because, among other things, the number of shares of Millendo's common stock issuable to Tempest's securityholders is determined based on Millendo's net cash balance on the business day prior to the Closing and the capitalization of Tempest and Millendo at the Closing, Millendo's securityholders cannot be certain of the exact number of shares that will be issued to (or reserved for issuance to) Tempest's securityholders when Millendo's stockholders vote on the proposals at the Board Meeting. The Exchange Ratio referenced above is an estimate only and the final Exchange Ratio will be determined pursuant to a formula described in detail in the Merger Agreement and in this proxy statement/prospectus.

In addition, as of the Effective time, each Millendo stock option that is outstanding and unexercised immediately prior to the effective time of the Merger, will remain outstanding in accordance with its terms including certain Millendo stock options that will accelerate and vest in accordance with its terms on Closing.

As of the Effective Time, each option to purchase shares of Tempest's common stock (a "Tempest Option") that is outstanding and unexercised immediately prior to the Effective Time granted under the Tempest 2011 and 2017 Equity Incentive Plans ("Tempest Plan"), or otherwise, whether or not vested, will be, along with the Tempest Plan, assumed by Millendo and will become an option to purchase solely that number of shares of Millendo's common stock equal to the product obtained by multiplying (i) the number of shares of Tempest's common stock that were subject to such Tempest Option immediately prior to the Effective Time by (ii) the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Millendo's common stock. The per share exercise price for Millendo's common stock issuable upon exercise of each Tempest Option assumed by Millendo shall be determined by dividing (a) the per share exercise price of Tempest's common stock subject to such Tempest Option, as in effect immediately prior to the Effective Time, by (b) the Exchange Ratio, and rounding the resulting exercise price up to the nearest whole cent. Any restriction on the exercise of any Tempest Option assumed by Millendo will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such Tempest Option shall otherwise remain unchanged.

Furthermore, each warrant to purchase Tempest's common stock ("Tempest Warrant") that is outstanding and unexercised immediately prior to the Effective Time, whether or not vested, will be converted into and become a warrant to purchase (and Millendo shall assume each such Tempest Warrant in accordance with its terms) solely that number of shares of Millendo's common stock equal to the product obtained by multiplying (i) the number of shares of Tempest Common Stock that were subject to such Tempest Warrant immediately prior to the Effective Time by (ii) the Exchange Ratio, and rounding the resulting number down to the nearest whole number of shares of Millendo's common stock. The per share exercise price for Millendo's common stock issuable upon exercise of each Tempest Warrant assumed by Millendo shall be determined by dividing (a) the

per share exercise price of Tempest's common stock subject to such Millendo Warrant, as in effect immediately prior to the Effective Time, by (b) the Exchange Ratio, and rounding the resulting exercise price up to the nearest whole cent. Any restriction on the exercise of any Tempest Warrant assumed by Millendo will continue in full force and effect and the term, exercisability, vesting schedule and other provisions of such Tempest Warrant shall otherwise remain unchanged.

Pre-Closing Financing

Concurrently with the execution and delivery of the Merger Agreement, certain parties have entered into agreements with Tempest pursuant to which they have agreed, subject to the terms and conditions of such agreements, to purchase prior to the consummation of the Merger shares of Tempest common stock for an aggregate purchase price of approximately $28.1 million, net of issuance costs of $1.9 million. The consummation of the transactions contemplated by such agreements is conditioned on the satisfaction or waiver of the conditions set forth in the Merger Agreement. Shares of Tempest common stock issued pursuant to this financing transaction will be converted into shares of Millendo common stock in the Merger in accordance with the Exchange Ratio.

2. Basis of Presentation

The accompanying unaudited pro forma condensed combined financial information was prepared in accordance with Article 11 of SEC Regulation S-X. The unaudited pro forma condensed combined balance sheet as of December 31, 2020 was prepared using the historical balance sheets of Tempest and Millendo as of December 31, 2020 and gives effect to the Merger as if it occurred on December 31, 2020. The unaudited pro forma combined statements of operations for the year ended December 31, 2020 give effect to the Merger as if it occurred on January 1, 2020 and were prepared using the historical consolidated statement of operations and comprehensive income of Millendo and Tempest for the year ended December 31, 2020.

For accounting purposes, Tempest is considered to be the acquiring company and the Merger is expected to be accounted for as a reverse recapitalization of Millendo by Tempest because on the Merger date, the pre-combination assets of Millendo are expected to be primarily cash and other non-operating assets.

For purposes of these pro forma financial statements, this estimated purchase price consideration consists of the following:

Estimated number of shares of the combined company to be owned by Millendo stockholders (1)		19,043,034
Multiplied by the assumed price per share of Millendo common stock (2)	$	1.14
Estimated fair value of shares of combined company to be owned by Millendo stockholders	$	21,709,059
Estimated fair value of assumed Millendo equity awards based on precombination service (3)		177,149
Estimated fair value of assumed Millendo warrants		4,010
Estimated purchase price	$	21,890,218

(1) Reflects the number of shares of common stock of the combined company that Millendo equity holders would own as of the Closing pursuant to the Merger Agreement. This amount is calculated, for purposes of this unaudited pro forma condensed combined financial information, based on shares of Millendo's common stock outstanding as of April 29, 2021.

(2) Reflects the assumed price per share of Millendo common stock, which is the closing trading price of Millendo's common stock on April 29, 2021. The actual purchase price will fluctuate until the effective date

of the transaction. A 10% increase (decrease) to the Millendo share price would increase (decrease) the purchase price by $2.2 million.

(3) Reflects the estimated acquisition-date fair value of the assumed Millendo's equity awards attributable to precombination service (which amount will be determined based on the closing trading price of Millendo common stock on April 29, 2021, the number of Millendo equity awards outstanding on this date, and the period of service provided by the holders of the awards prior to the Merger closing date in 2021).

The purchase consideration for the net assets of Millendo will be determined based on a net cash calculation prior to Closing and will be adjusted dollar-for-dollar by the amount that the net cash amount is greater than $18.7 million or less than $15.3 million. The actual purchase consideration will vary based on the net cash calculation prior to Closing, the Exchange Ratio, and Millendo share price at Closing as described above and that difference could be material. As such, the estimated purchase consideration reflected in these unaudited pro forma condensed combined financial information does not purport to represent what the actual purchase consideration will be when the Merger is completed.

Under reverse recapitalization accounting, the assets and liabilities of Millendo will be recorded, as of the completion of the Merger, at their fair value. No goodwill or intangible assets are expected to be recognized and any excess consideration transferred over the fair value of the net assets of Millendo following determination of the actual purchase consideration for Millendo will be reflected as a reduction to additional paid-in capital. Consequently, the financial statements of Tempest reflect the operations of the acquirer for accounting purposes together with a deemed issuance of shares, equivalent to the shares held by the former stockholders of the legal acquirer and a recapitalization of the equity of the accounting acquirer. The accompanying unaudited proforma condensed combined financial information is derived from the historical financial statements of Millendo and Tempest, and include adjustments to give pro forma effect to reflect the accounting for the transaction in accordance with U.S. GAAP. The historical financial statements of Tempest shall become the historical financial statements of the combined company.

The unaudited pro forma condensed combined financial information does not include the impact of any revenue, cost or other operating synergies that may result from the Merger or any related restructuring costs that may be contemplated and does not give effect to the proposed Millendo Reverse Stock Split because the proposed reverse stock split is a range, is not definitive and is subject to approval by Millendo's stockholders.

To the extent there are significant changes to the business following completion of the Merger, the assumptions and estimates set forth in the unaudited pro forma condensed consolidated financial information could change significantly. Accordingly, the pro forma adjustments are subject to further adjustments as additional information becomes available and as additional analyses are conducted following the completion of the Merger. There can be no assurances that these additional analyses will not result in material changes to the estimates of fair value.

3. Shares of Millendo Common Stock Issued to Tempest Stockholders upon Closing of the Merger

Prior to the Merger, all outstanding shares of Tempest's convertible preferred stock are expected to be converted into Tempest common stock, which will be exchanged for shares of Millendo common stock based on the Exchange Ratio determined in accordance with the Merger Agreement. The estimated Exchange Ratio for purposes of the unaudited pro forma condensed combined financial information was derived on a fully-diluted basis as of April 29, 2021 using a stipulated value of Tempest of approximately $158.4 million (including the Pre-Closing Financing discussed above) and of Millendo of approximately $36.0 million. The estimated number of shares of common stock that Millendo expects to issue to Tempest's common and preferred stockholders as of April 29, 2021 (ignoring rounding of fractional shares) is determined as follows:

Shares of Tempest's common stock	51,769,792
Shares of Tempest's convertible preferred stock	114,686,731
	166,456,523
Exchange Ratio	0.488
Estimated shares of Millendo common stock expected to be issued to Tempest stockholders upon Closing	81,230,783

As the reverse stock split is a range and is not definitive and will occur immediately prior to the consummation of the Merger, the Exchange Ratio and estimated shares of Millendo's common stock issued to Tempest's security holders have not been adjusted to give retrospective effect to the reverse stock split.

4. Proforma Adjustments

The following unaudited pro forma condensed combined financial information has been prepared in accordance with Article 11 of Regulation S-X as amended by the final rule, Release No. 33-10786 "Amendments to Financial Disclosures about Acquired and Disposed Businesses." Release No. 33-10786 replaces the existing pro forma adjustment criteria with simplified requirements to depict the accounting for the transaction ("Transaction Accounting Adjustments") and present the reasonably estimable synergies and other transaction effects that have occurred or are reasonably expected to occur ("Management's Adjustments"). Millendo has elected not to present Management's Adjustments and will only be presenting Transaction Accounting Adjustments in the following unaudited pro forma condensed combined financial information.

Based on Tempest management's review of Millendo's summary of significant accounting policies, the nature and amount of any adjustments to the historical financial statements of Millendo to conform to the accounting policies of Tempest are not expected to be significant. The pro forma adjustments, based on preliminary estimates that could change materially as additional information is obtained, are as follows:

A. To reflect $28.1 million, net of issuance costs of $1.9 million, in proceeds to be received by Tempest, in connection with the consummation the Pre-Closing Financing. The Merger is contingent upon the Pre-Closing Financing, which is expected to close concurrent with the Merger, at or prior to the Closing. If the Pre-Closing Financing does not close, Tempest and Millendo are not required to complete the Merger.

B. To reflect preliminary estimated transaction costs of $3.3 million in connection with the Merger, such as adviser fees, legal, and accounting expenses that are expected to be incurred by Tempest as an increase in accrued liabilities and a reduction to additional paid-in capital in the unaudited proforma condensed combined balance sheet.

C. To reflect preliminary estimated transaction costs of $5.5 million in connection with the Merger, such as adviser fees, legal, directors and officers liability insurance, and accounting expenses, that are expected to be incurred by Millendo as an increase in accrued liabilities and accumulated deficit in the unaudited proforma condensed combined balance sheet.

D. Compensation expense of $2.2 million related to severance, retention and transaction bonuses resulting from preexisting employment agreements that will be payable in connection with the Merger is reflected as an increase to accumulated deficit and accrued liabilities in the unaudited pro forma condensed combined balance sheet. The pro forma adjustments exclude certain termination benefits incurred in connection with Millendo's January 2021 corporate restructuring plan.

E. To reflect the adjustments to account for operating lease liabilities and right-of-use assets at their fair values as of December 31, 2020 in the unaudited pro forma condensed combined balance sheet.

F. To reflect the conversion of 114,686,731 shares of Tempest's convertible preferred stock into shares of Tempest's common stock immediately prior to the Merger.

G. To record (i) the conversion of Tempest's convertible preferred stock into 114,686,731 shares of common stock, (ii) issuance of 35,258,582 shares in connection with the consummation the Pre-Closing Financing (iii) the accrual of transaction costs associated with the Merger, (iv) the payment of severance and retention bonuses in connection with the Merger, (v) post combination compensation expense of $0.3 million related to Millendo options recognized upon the Closing, (vi) the elimination of Millendo's historical equity, including 18,999,701 outstanding shares of common stock at their par value of $0.001 million, $0.4 million of accumulated other comprehensive income and $277.7 million additional paid-in capital, (vii) the exchange of outstanding Tempest's common stock into 81,230,783 shares of Millendo's common stock based on the assumed Exchange Ratio for purposes of these pro forma condensed combined financial information, and (viii) the effect of the reverse recapitalization of Millendo for a total of $33.1 million, which is the net assets of Millendo as of December 31, 2020.

(amounts in thousands, except share amounts)	Common Stock				Additional Paid-In-Capital	Accumulated Deficit	Acccumulated other comprehensive income	Total Stockholders' Equity
	Tempest Shares	Amount	Millendo Shares	Amount				
Conversion of outstanding Tempest's convertible preferred stock into common stock	114,686,731	115	—	—	86,592	—	—	86,707
Payment of D&O insurance tail	—	—	—	—	—	(2,500)	—	(2,500)
Payment of transaction costs	—	—	—	—	(3,300)	(3,025)	—	(6,325)
Payment of severance and retention bonuses	—	—	—		—	(2,187)	—	(2,187)
Post combination stock-based compensation costs	—	—	—	—	257	(257)	—	—
Elimination of Millendo's historical equity carrying value	—	—	(19,043,034)	(19)	(277,647)	245,060	(452)	(33,058)
Exchange of outstanding Tempest's common stock into Millendo's common stock based on the assumed Exchange Ratio	(166,456,523)	(165)	81,230,783	80	85	—	—	—
Reverse recapitalization of Millendo	—	—	19,043,034	19	33,039	—	—	33,058
Pre-Closing Financing	35,258,582	35	—	—	28,015	—	—	28,050
Fair value remeasurement of right-of-use assets	—	—	—	—	215	—	—	215
Pro forma adjustment	(16,511,210)	(15)	81,230,783	80	(132,744)	237,091	(452)	103,960

H. The preliminary estimated transaction cost of $5.5 million in connection with the Merger, such as adviser fees, legal, directors' and officers' liability insurance, and accounting expenses that are expected to be incurred by Millendo are reflected as if incurred on January 1, 2020, the date the Merger occurred for the purposes of the unaudited pro forma condensed combined statement of operations. This is a non-recurring item.

I. Compensation expense of $2.2 million related to severance, retention and transaction bonuses resulting from preexisting employment agreements that will be payable in connection with the Merger is reflected as if incurred on January 1, 2020, the date the Merger occurred for the purposes of the unaudited pro forma condensed combined statement of operations. This is a non-recurring item. The pro forma adjustments exclude certain termination benefits incurred in connection with Millendo's January 2021 corporate restructuring plan.

J. To reflect the post combination compensation expense of $0.3 million related to Millendo's options recognized upon the Closing for the purposes of the unaudited pro forma condensed combined statement of operations. This is a non-recurring item.

K. The pro forma combined basic and diluted earnings per share have been adjusted to reflect the pro forma net loss for the year ended December 31, 2020. In addition, the weighted average shares outstanding for the period have been adjusted to give effect to the issuance of Millendo's common stock in connection with the Merger as of April 29, 2021. As the combined company is in a net loss position, any adjustment for potentially dilutive shares would be anti-dilutive, and as such basic and diluted loss per share are the same. The following table presents the calculation of the pro forma weighted average number of common stock outstanding without giving effect to the proposed reverse stock split:

	Year Ended December 31, 2020
Weighted average Tempest shares outstanding	14,539,178
Weighted average shares of Tempest redeemable convertible preferred stock	112,169,608
Shares issued upon Pre-Closing Financing	35,258,582
	161,967,368
Weighted average Tempest shares outstanding adjusted for the Exchange Ratio	79,040,076
Weighted average Millendo shares outstanding	18,862,537
Pro forma combined weighted average number of shares of common stock—basic and diluted	97,902,613